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Vol. 6 No. 10 October 1949

ATOMIC ENERGY IN CLINICAL MEDICINE

HENRY J. KLAUNBERG, Ph. D.
Executive Editor

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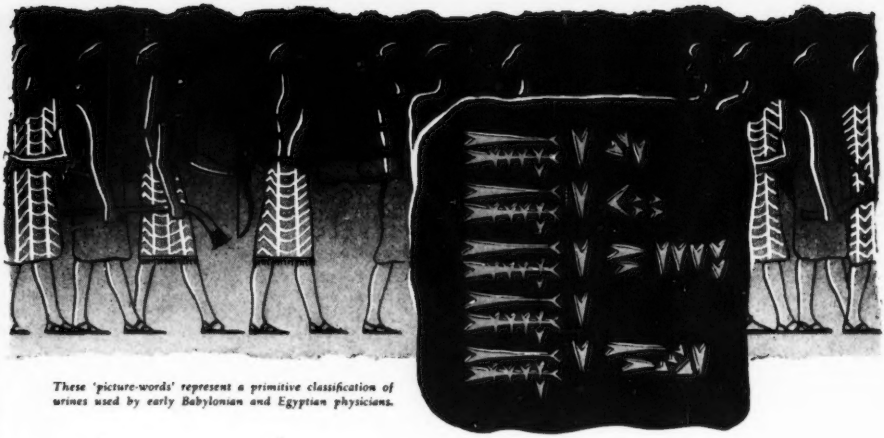

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This material, covering all branches of medicine, is presented for easy reading and quick reference under the following headings:

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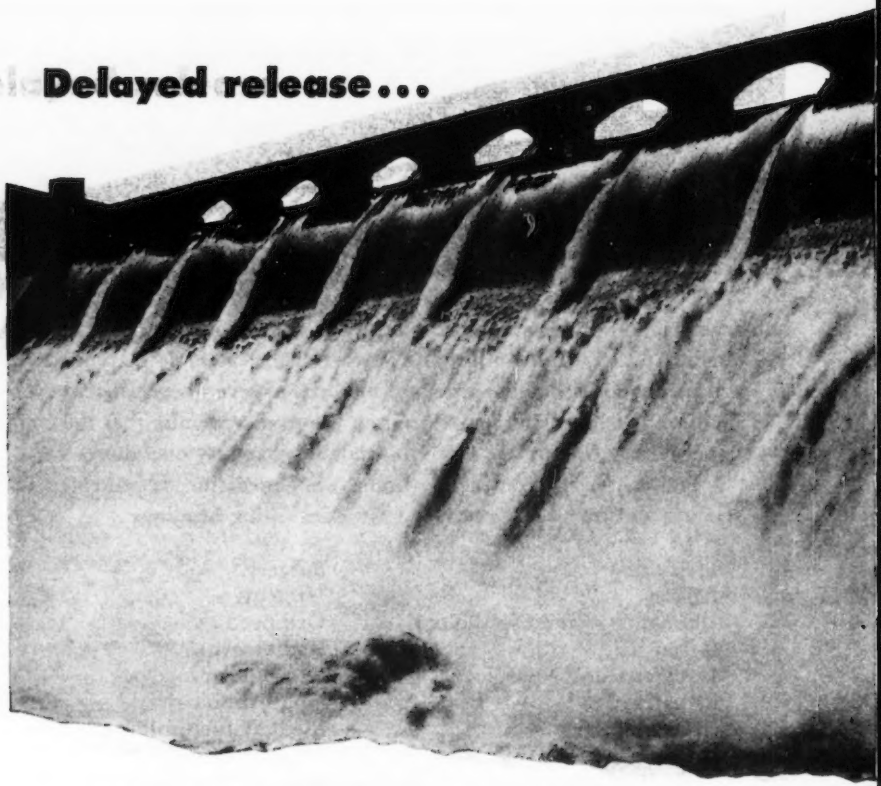

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GENERAL PRACTICE CLINICS

October 1949

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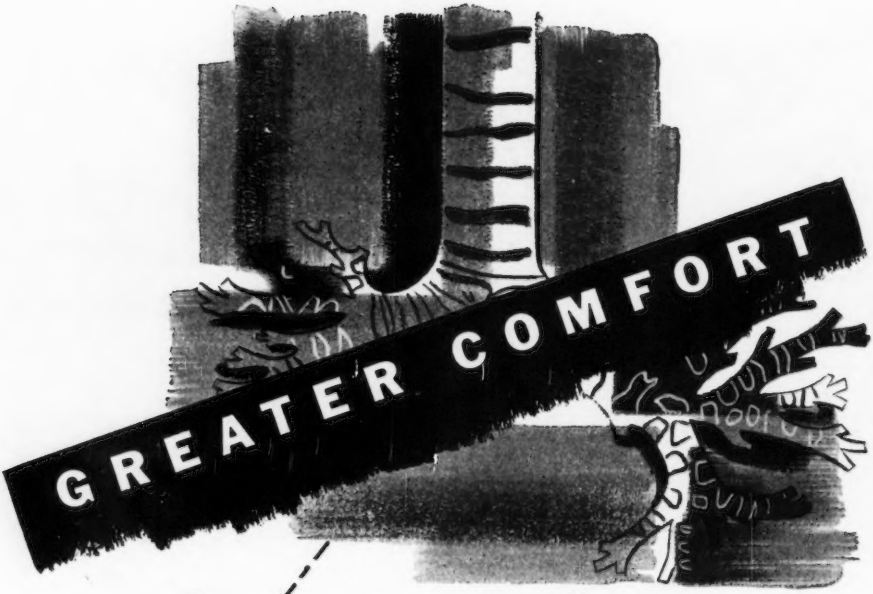

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GENERAL PRACTICE CLINICS

Vol. 6 No. 10 October 1949

3. BENEFITS FROM ATOMIC ENERGY *

Atomic energy's great gift to the sciences of biology and medicine is quantities of low-priced radioactive isotopes of the common elements that are important in the life processes of plants, animals, and men. All radioisotopes throw off rays or particles—carbon 14 and phosphorus 32, for example, emit beta particles; iodine 131, and sodium 24 radiate both beta particles and gamma rays—and it is these emissions which give them their special value to science.

Radiation that destroys the cells of cancer is one of the few effective means of controlling some forms of the disease. Scientists have used radioiodine to treat people with an over-active thyroid gland, or with cancer of the thyroid, because the gland absorbs almost all the iodine taken into the body. They have used radioiodine similarly to trace out seats of new cancers that have spread from a thyroid root.

Surgeons have used radiophosphorus to locate brain tumors accurately during a dozen or more successful operations, because the tumor has a far greater avidity for phosphorus than does the normal brain tissue. The same radioisotope, phosphorus, has curbed the excessive production of red blood corpuscles in patients with the disease *polycythemia vera* and has gained relief for patients with *leukemia*, a disease marked by cancerous overproduction of white blood corpuscles.

New Knowledge From Isotopes

In clinical research with patients, physicians must use radioisotopes with great caution and carefully select the element used according to the type of emission it radiates, the length of its radioactive life, the place to which it goes in the body and its toxicity as a chemical. However, minute quantities are being used, for example, in assay-

* Continued from September 1949 issue of *General Practice Clinics*, Vol. 6, No. 9.

ing the amount of certain critical minerals—the *trace elements*—which a patient may lose after a severe operation. It has never before been possible to estimate closely how much potassium was in a man's body, hence to know the percentage of this essential substance he is losing. Now, by making a minuscule injection of radiopotassium, then measuring the ratio of this isotope to ordinary potassium in the patient's excreta, doctors can make a very precise calculation.

Isotope Dilution Test

The method used in this test parallels that which might be used to estimate the number of white beans in a five-gallon jar. The estimator could throw a hundred black beans into the jar, mix the contents thoroughly, and then take a random sample. If the sample contained two black beans and a thousand white beans, he could estimate that there would be 500 times as many white beans as black beans.

In the potassium test, the radiolabeled atoms are the "black beans." By this device, scientists at Harvard University have determined that potassium in the human body is about one part in 500 by weight.

The dosage of radiopotassium used in the tests was infinitesimal. Scientists have calculated that a millicurie of carbon 14 contained in one hundred-thousandth of an ounce of the element can be accurately measured when spread through as much as 10 tons of animal tissue—in, for example, 20,000 guinea pigs. This amount—a *millicurie*—shows 37 million nuclear break-downs every second and at least that number of radio emissions. The amount of radiopotassium used to measure a patient's loss of this trace element thus need be only a very small fraction of one hundred-thousandth of an ounce.

Activation Analysis

Radioactivity has been used in still another way to determine how much of certain trace elements our bodies contain, even when the amount is too small to be measured by ordinary chemical means. A portion of body fluid is reduced to an ash, then subjected to irradiation by slow neutrons of known velocity. The metals, cobalt, or copper for instance, are then separated out of the ash chemically. Scientists at the Radiation Laboratory, University of California, were then able to make a very precise measurement of the copper and cobalt in the body.

All of these uses of radioelements constitute new techniques. The value to science of the tracer technique has been described as equal to that of the microscope. Like the microscope, tracers are useful in nearly all kinds of scientific inquiry.

Isotope Program

When the operation of the giant nuclear reactors first made radiochemicals available in large quantities at comparatively low prices, the Manhattan District determined to encourage their widest possible use in research of all kinds and the Commission has expanded this program. The Commission's charter directs such support and, in the language of the Atomic Energy Act of 1946, the Commission "is authorized and directed to make arrangements (including contracts, agreements and loans) for the conduct of research and development activities relating to . . . (3) utilization of fissionable and radioactive materials for medical, biological, health or military purposes; (4) utilization of fissionable and radioactive materials and processes entailed in the production of such materials for all other purposes, including industrial uses . . . ."

Since its operations began, in January 1947, the Commission has authorized contracts and research fellowships and assisted in the purchase of equipment and establishment of laboratories where radioisotopes could be used. It has financed projects using the "tracer" technique. It has produced and priced isotopes on the basis of actual production cost, without charges on capital investment or for depreciation, and has reduced prices when feasible. All isotopes used in cancer research and therapy are made available free of production costs. At Argonne's Radiobiology Experiment Station, radioactive compounds useful in research are being synthesized in growing plants and will be distributed as part of the isotope program. Oak Ridge, Berkeley Radiation Laboratory, Los Alamos, and three private firms are also synthesizing radio-labeled compounds for tracer research. (See Appendix 8 for a report on the Argonne station.) Training programs, conducted at Oak Ridge, are helping qualified scientists to acquire the new techniques. More than 240 have been trained, and 56 others have taken special medical courses. The 30-day seminars which include 32 persons each, are going on continuously.

Partly as a result of this program, use of radioisotopes has increased enormously since January 1947. In terms of dollar value of sales, the

INCREASED USE OF RADIOISOTOPES

Domestic Program	*Aug. 1946 to Dec. 1946*	*Jan. 1949 to June 1949*	*Aug. 1946 to June 1949*
Shipments	246	1, 817	6, 359
States receiving (including Hawaii, District of Columbia)	23	36	41
Institutions receiving	92	199	309
Revenue from non-AEC sales	$31, 264	$151, 827	$513, 505

increase as of June 1949, was nearly 400 percent; in terms of numbers of institutions using isotopes in research, 100 percent.

The program for assistance on tracer research now concerns the following fields:

(*a*) Projects that increase knowledge of the effects of radiation on plants and animals. In this field, it is important to investigate also those normal life processes which are affected by radiation and of which too little is known, such as those involving the blood, cellular build-up and break-down, genetics, bone formation, growth, and enzyme cycles.

(*b*) Projects on the frontiers of knowledge which promise to broaden the scope of basic science.

(*c*) Projects which promise to develop new techniques, instruments, compounds and similar items, useful in radioisotope research.

(*d*) Projects which, in universities or laboratories not previously interested but adequately qualified, will help to broaden the Nation's research with the use of radioisotopes.

The program, moreover, will continue its indirect support throughout the field of nuclear research (*a*) through training in nuclear fields, (*b*) through promoting research in new techniques and instrumentation and encouraging the manufacture of instruments (*c*) through laboratory work on synthesizing compounds of radioisotope needed for research and encouragement of private producers.

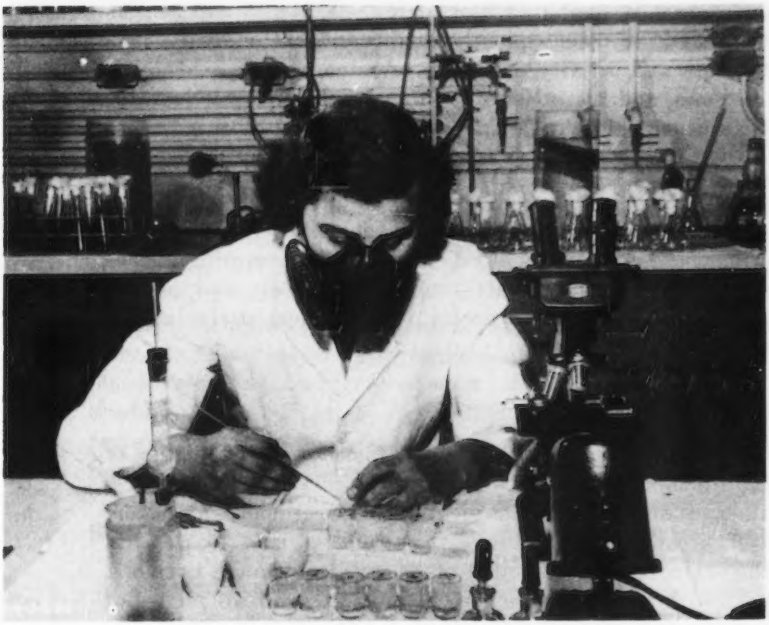
A. TRACER RESEARCH

Over 300 institutions in 39 states, the District of Columbia and Hawaii, are using radioisotopes for scientific research. The inquiries financed by the Commission make up only a small fraction of this total. Its 34 projects in biology and medicine are directed primarily toward filling gaps in the total national program, and most of them already are focused within the boundaries of the policy as formulated here.

Many Commission projects are laying the groundwork for an understanding of the effects of radiation by seeking to learn the normal structures and dynamics of the body.

The Body's Building Blocks

The body, in its functioning, uses a variety of building blocks. *Proteins*—complex molecules manufactured in the body from amino acids.



Worker at the Los Alamos Scientific Laboratory preparing samples containing radioactive carbon (carbon 14) for use in tracer research. The barium carbonate samples were made from carbon dioxide given off by bacterial cultures grown on nutrient material containing carbon 14.

The enzymes, catalysts of cellular reactions and some hormones also are proteins, and proteins are required to bind vitamins into useful compounds. *Carbohydrates*, essential fuels for the body, are burned to produce energy and maintain life and also enter importantly into body structure. *Lipids*—the fats and fatlike substances, which are at once a source of energy, a tool of regeneration and a component of certain hormones. *Nucleic acids*, whose composition is only partly understood, are tied in a way not yet explained to a protein that has not yet been defined, to form the largest molecules of all, the nucleoproteins, making up the nuclei of the cells that form the subtance of the body.

In addition to these building blocks, other important key substances include the various *blood* constituents and the *electrolytes*—such minerals as potassium, sodium, and calcium.

Full understanding of the hows and whys of the behavior of many of these substances must often wait on determining exactly what they are. Diseases, or radiation, shatter some of these substances, alter

others, render some incapable of functioning. This also will be difficult to understand—and consequently hard to prevent or treat—until the basic nature and activity of lipids, proteins, nucleic acids, electrolytes, enzymes, and hormones are better defined by basic research of the types sponsored by the Commission.

BLOOD

An example of the attack upon these problems is the studies on the essential constituents in the blood. The blood, containing plasma and cells, is the circulating distributor of chemicals and oxygen throughout the body. It lends itself to biochemical study because of the ease of obtaining samples.

A Study of Anemia

Anemia is a disease characterized by a deficiency in the quality or quantity of the blood. Dosages of iron often correct the deficiency, but certain types of anemia do not yield to this treatment. Occasionally this type is caused by a failure of the pituitary gland, located just beneath the brain, to secrete enough of its essential growth hormone.

Treatment with hormones has been found to correct all phases of anemia in the pituitary cases except for the deficiency in the hemoglobin—the coloring matter of the red corpuscles which transmits oxygen to the cells and carries away the oxidation waste products to the lungs, and which uses iron as one of its constituents. At Boston University, scientists of the School of Medicine removed the pituitary gland of laboratory rats, injected the radioactive iron, then traced the distribution of the iron through their organs and bodies and compared this distribution with that of normal rats. They concluded that the hemoglobin deficiency was not caused by lack of iron.

By studying a rare type of anemia in laboratory animals, scientists are expanding our fundamental knowledge of the manufacture of blood.

The scientists therefore pushed their experiment into the other constituents of hemoglobin—in particular the protein fraction. They found that by feeding the rats a high protein diet, coupled with hormone therapy, they could prevent anemia even after removal of the pituitary gland. Accordingly, they are now preparing to use radioactive carbon to label glycine, one of the amino acids used by the body to manufacture the hemoglobin protein, so as to trace this phase of blood metabolism.

The scientists feel that their investigation has reached a stage which will permit them to try this treatment on human patients

in the clinics. High protein diet added to present hormone therapy, they suggest, may succeed in overcoming anemias that do not yield to iron treatment.

Measuring Body Liquids

At the Radiation Laboratory, University of California, red blood cells are taken from the body, labeled with radiophosphorus and then reinjected to determine the speed with which the labeled substance mixes with the total blood. The time for complete mixing varies widely with individuals, it was found, and requires between 5 and 15 minutes. The interval was definitely longer in patients with heart diseases. The rate of disappearance of sodium and iodine from the blood stream, as compared with the total surface of tissue was measured by tracers. These two investigations will make possible a satisfactory measurement of such factors as blood volume, the amount of fluid outside of cells, total body water and total body sodium.

The total volume of blood in the human body is of importance in a number of circumstances. For example, the increase in volume of red cells which takes place in polycythemia vera will eventually lead to death through blood clots, apoplexy or leukemia. In contrast, in patients who are to undergo a major operation, it is important to know if there is any decrease in the amount of blood. The method of measurement cited has proved of value in such studies.

Metals in Blood Metabolism

Iron and zinc both enter importantly into the metabolism of red and white blood cells. Discovering the activity of these "trace" metals therefore may offer important information both in anemia and in leukemia.

A group of physicists, chemists, and physicians, collaborating in studies of these diseases at the Massachusetts Institute of Technology since 1941, is currently using radioisotopes of iron and zinc in its work under a contract with the Commission.

Iron. Some 200 young men volunteered to receive injections of radioactive iron so weak that the radiation was below the levels which human beings can safely tolerate. Tests of these young men after 6 months showed no ill effects from the irradiation.

Measurements of iron in the human system, by means of the radioactive isotopes, show that the body loses only a very small fraction of this metal and that the daily requirement is only about one to two one-thousandths of a gram, but even under forced feeding the system

assimilates very little. However, the human system salvages about 90 to 95 percent of the iron when red cells die and reuses this iron to form new cells. These facts indicate why blood transfusion is such an effective means of administering iron. They point also to factors which must be considered in management of a national blood donor program. Iron therapy is necessary for the donors and repeated donations, without such treatments, will produce anemia.

Experiments have also shown that new red cells in the bone marrow can assimilate iron for a few days, but that mature red cells cannot. Folic acid and liver extracts increase the ability of the young cells to take up iron.

At Brookhaven National Laboratory, scientists have determined that iron, an important constituent of the red blood cells, is used in almost equal amounts by another body pigment, the cytochrome, and that even larger quantities are used by a constituent of the muscles suspected to be the muscle hemoglobin.

Zinc. In the experiments at M. I. T. with zinc, scientists found that this metal apparently plays an important role in the life cycle of the white blood cell. Large quantities of living white cells, tagged with radiozinc, are being injected into dogs in an effort to trace this life cycle. A full understanding of the process may throw some light on the mechanism of overproduction of white cells in leukemia. They have demonstrated that leukemic white blood cells have a pronounced deficiency in zinc.

Chromium. Using radioactive metals to follow "trace" elements, Harvard Medical School scientists have found that chromium enters into many tissues of the body. It penetrates blood cells within a matter of minutes, and stays firmly bound, possibly for the life of the cell. A program under way now is seeking to determine which cells and, if possible, what portion of each cell the chromium enters. Other research is tracing the function of calcium in the nerves, and the role of zinc in insulin formation.

Proteins in Blood Stream

The proteins of the blood assist in blood clotting, form a part of the hemoglobin molecule, hold fluid in the blood vessels, and are a part of the body's defenses against infection.

At the University of Rochester, scientists used radiocarbon to label one of the amino acids, lysine, which is indispensable to life and growth. By tracing the labeled lysine, it was discovered that the body used it to form other amino acids, to build other proteins of the blood plasma, and to build red corpuscles.

As a result of the studies, other scientists suggest that labeled red cells be used to test methods of handling and storing whole blood for transfusions.

Further studies showed that, in the dogs used in the laboratory, plasma proteins have a very rapid turnover. About half the protein in the dog's plasma system is renewed within 3 days. This suggests that plasma proteins play a very important part in the entire protein economy of the body, and they may represent preformed "building blocks" used for tissue. Scientists are now using tracer-proteins to discover what happens to these protein molecules in a plasma transfusion.

These studies are of value not only in the problem of radiation injury but also in the cancer field. For example, in cancer of the stomach there is often an early fall in the level of the plasma proteins, the mechanism of which is not understood. A number of other conditions, such as severe burns and kidney disease, require the administration of substances to replace or maintain the plasma proteins.

A Study of Loss of Body Salts

Electrolytes, the mineral salts essential to health and to many body processes, often are lost rapidly after severe injury, surgical operations or generalized severe infection. These changes in body chemistry are of the greatest importance to survival, healing and convalescence.

Recently it has been learned that many of the deaths from acute diarrhea in infants are due to a marked fall in the potassium content of the body. There is a substantial potassium loss in diabetic acidosis which has only recently been recognized. Studies in this field will assist in clarifying the perplexing problems concerned in the mechanism of this loss. It is probable that there are similar changes in individuals who are suffering from radiation injury.

Studies in this field during the last 2 years at Harvard Medical School, Peter Bent Brigham Hospital and Massachusetts General Hospital have concentrated on cells' loss of potassium and an apparent penetration of sodium into the cells, although sodium is normally found only outside of cells.

Potassium losses. Radioisotopes are used in two ways in this clinical research. Radiopotassium has been used (as described on p.494) to determine that people may lose up to 25 percent of total body potassium after severe surgery. Radiosodium is also being injected before operation in certain cases, so as to measure the amount that is retained in the body fluids. This will indicate the amount that has been absorbed into the cells.

A nonradioactive variety of water—heavy water—has been used in this same group of experiments to determine, by an isotope dilution method similar to that used with potassium, the amount of water in the body. The method is much more difficult since the experimenters are unable to use the radioactive counter, and must determine the presence of heavy water by extremely delicate and accurate tests. They have calculated that the amount of water varies widely with the body build of the patient, particularly in relation to the amount of fat. The total amount of water may range anywhere from 60 to 80 percent of total body weight.

How Infection Affects Organs

Scientists at Bowman Gray School of Medicine, Wake Forest College, are using radioactive sodium and potassium to study the effects upon the organs of such infectious diseases as Rocky Mountain Spotted Fever. In this disease, the membranes of blood vessels and individual cells are so affected that water and salt can pass through them more readily than in normal individuals. In severe infections, even proteins and red blood corpuscles can pass through the membranes. Standard techniques in this research have given only limited information. It is hoped that the use of radiotracers will yield more detailed information.

PROTEINS

The way in which proteins—the substance of the structure and the engines of the body—are formed has long been hidden. Synthesis has been observed hitherto only in the living animal or plant. To learn how the process occurs investigators must be able to make the process go on outside the body in reaction vessels. A project at California Institute of Technology succeeded in producing protein synthesis outside the body in glass receptacles. Rabbit bone marrow cells, rat diaphragm, and guinea pig liver were used. All three tissues take up a number of different amino acids, among them glycine, leucine, and lysine which are building blocks of proteins. Since each of these acids has been tagged with radiocarbon, the protein molecules formed are labeled in three places. This fact helps to locate the position of other amino acids and to work out a detailed pattern of amino acids in protein. It is variation in pattern which underlies such differences as antibody behavior, structure, and catalytic activity.

It was found that the incorporation of amino acids into the proteins of these tissues can be made to proceed outside the body at the same rates and under similar physiological conditions as within the body.

The process requires energy obtained from the burning of food materials.

Analyzing the process further investigators found that the different components of the cell, the nucleus and organized molecules in the cell outside the nucleus, participate in the process, each in a different way. One set of molecules behaves like an engine, it drives the machine. Another set is the machine which does a specific job provided it is driven by the engine.

It was possible also to follow in detail the breakdown of lysine. The first step was the formation of a hitherto unknown amino acid, aminoadipic acid. Research investigators also found what appears to be one of the most important subunits of animal protein—a peptide, or union of amino acids, present in the liver of all animals. It contains nearly all the amino acids and takes up the tagged acids rapidly. This protein component is a major product of digestion of animal protein foods.

Radiocarbon is being used at Oregon State College to trace the relationship of carbohydrates to amino acids, and further to attempt to determine whether as is believed, certain amino acids are related to the water-soluble vitamin, pantothenic acid, which is the "anti-gray hair" part of the vitamin B complex.

LIPIDS

The lipids include fats and fat-like substance formed in the body from the food we eat; it is their "combustion" that supplies a good part of the body's energy. An understanding of the way the lipids are formed and broken down into the products that are "burned" by oxidation for energy and of the effect upon this process of certain drugs and diseases is of the utmost importance to a clear picture of human life processes. It has particular importance to people suffering from diabetes.

Radiophosphorus is used at Bowman Gray School of Medicine, Wake Forest College, to study the formation of certain liver fats which contain phosphorus. A number of powerful drugs failed to affect the process appreciably, though some reduction in the formation of the fats resulted from slowing thyroid activity. Apparently, the liver has the power to continue production of these fats under very adverse conditions. However, very marked decreases were observed after administration of compounds which presumably reduce the availability of the fat-building materials. The drugs also are being used to clarify the exact pathways through which the phosphorus fats are formed in the liver.

These processes may be important for understanding the causes of certain liver diseases, and the formation of the phosphorus fats in the blood is being studied in human patients.

In another study, the harmful effects of radioactive phosphorus are being investigated to find out whether changes in diet may increase the resistance of animals to the harmful effects of internally administered radioactive elements.

NUCLEIC ACID MOLECULES

The normal functioning of the cell and of the entire living body depends upon a very carefully balanced working relationship among the various biological factors previously discussed. If we were to select one type of compound which could be designated as the keystone of life, nucleic acids and nucleoproteins would be the leading candidates for the honor. Nucleic acids are composed of simple organic nitrogen ring compounds, sugar molecules, and phosphorus groups, linked together into chains to form very complex supermolecules. These nucleic acid supermolecules in turn are linked to protein supermolecules to form nucleoprotein.

The nucleoprotein molecule is at the borderline between the truly living material and the nonliving. Certain of the plant and animal viruses are known to be pure nucleoproteins. The chromosomes which control the hereditary characteristics of the individual and the race are nucleoproteins. Our present knowledge of the cancer problem indicates that abnormal influences may cause the nucleoprotein material in the cell to go wild and to reproduce itself in an uncontrollable manner.

Thus it is to be seen that many fields for which the Commission has responsibility—radiation effects, genetic effects and cancer—are intimately connected with the nucleoproteins.

Program on Nucleic Proteins

In order to increase our scientific understanding of nucleoproteins and how they are affected by radiation, the Commission is sponsoring an extensive program, in its own and university laboratories, to synthesize the various building blocks of the nucleoproteins, to label them with radioactive isotopes and to follow their metabolic course in animals and other living organisms. It is only when we know precisely how these building blocks are put together and how their structure is altered by radiation and disease that we will be able to proceed soundly in the treatment of radiation effects.

Nucleic acid and growth. Research men at the University of Colorado are studying the activity of derivatives of nucleic acid in the system. These have been synthesized and techniques worked out for their use. Some are known to produce growth and small chemical changes in these molecules result in material that arrests growth. One phase of the research will investigate the results of such derivatives when applied to radiation-damaged cells.

Many of the research projects in other areas are related to the elements of the cell nucleus. At Harvard Medical School, for example, the effects of adrenal and pituitary hormones and of insulin in the formation of starch in muscle cells and its release through the action of acetic and pyruvic acid are being studied. Many other projects dealing with growth, proteins, genetics, and cancer also are related.

Study of Diabetic Processes

Ever since the discovery of insulin as a control for diabetes, attempts have been made to learn exactly which chemical reactions in the body are speeded up or slowed down by this substance. The primary chemical disturbance caused by undersecretion of insulin is, of course, a reduction in the body's ability to use sugar.

At Harvard Medical School radiosugar was made by growing bean plants in an atmosphere of radiocarbon dioxide or by using liver cells for a similar process of synthesis. This sugar, and the interaction of insulin, were then used in studying the chemistry of the muscle cells of rats which were diabetic, or which had hormone-secreting glands, the pituitary or the adrenals, removed.

These experiments showed that insulin increases the ability of the muscle not only to manufacture glycogen—the form in which sugar is stored in the cells—but also to burn sugar for energy. The hormones of the pituitary and adrenal retard, and insulin accelerates, the first step in use of sugar by the body. In this step, sugar is combined with phosphoric acid. Normally, this balance of slowing down and speeding up keeps the amount of sugar in the blood within the necessary narrow limits. In the diabetic person, with less insulin, the retarding substances hold down the use of sugar so that the body must obtain a greater amount of energy from the burning of fats. This excessive fat-burning produces acids and results, in uncontrolled diabetes, in a fatal accumulation of acids in the blood and tissues.

Acids in diabetes. Further experiments have probed into the acid processes of diabetes. Acetic and pyruvic acids are formed momentarily when fats and sugars are burned in the body. By tagging these

acids with radioisotopes, it was found their use is decreased in the muscle cells of a diabetic. Insulin brought back to normal the use of pyruvic acid, but acetic acid remained unburned. If the factor responsible for burning acetic acid—the factor missing, or greatly reduced in the diabetic—can be found and made available, the treatment of diabetes will be further improved.

Other Studies in Metabolism

By injecting into mice the B–2 vitamin as radioactive nicotinic acid or nicotinamide, scientists at Los Alamos Scientific Laboratory have shown that there is no essential difference in the way the body uses the two. Both are synthesized into Coenzymes I and II, substances into which nucleic acid splits when it breaks down. Incubation of the two vitamins with blood showed that, whereas nicotinic acid could be directly used by the red blood cells, nicotinamide could not, which may help explain why the latter is better in intravenous treatment.

The drug thiourea used in treatment of an overactive thyroid gland, was rendered radioactive and used to trace the drug's activity. After 72 hours, it was found that the concentration of thiourea in the thyroid was 80 percent greater than in other tissues.

Radioactive phosphorus is used as a tracer at Brookhaven National Laboratory to study its part in metabolism of sugars in the body. A great deal of work in this field has resulted in formulating what is known as the "phosphorylation cycle"—a description of the various intermediate steps in which phosphorus compounds are formed and used in the conversion of sugars into energy. Present experiments are concentrating on the liver's use of phosphorus in sugar metabolism. Normal conditions will be investigated first, afterwards those which exist in diabetic and cancer patients.

There is also some evidence that exposure to radiation reduces the capacity of the body cells to combine sugar derivatives with phosphate, and this will be investigated further.

B. DIAGNOSIS AND TREATMENT

In addition to serving as a tool for basic research into life processes, radioisotopes have proved valuable in laboratory and clinical studies of diseases, and are being used also in diagnosis and in treatment.

Isotopes in Diagnosis

Some of the most dramatic and striking results in medicine today are obtained from treatment to correct under- or over-secretion by the thyroid and the sex glands.

In diagnosing illnesses resulting from lack of hormones, extremely delicate techniques are necessary since these substances are effective in dilutions of one part in 10 million. Radio-tagged elements are used at Yale University School of Medicine, in connection with microscopic methods, to measure secretion of the sex hormones; radioiodine in the case of the thyroid. In one case, a half teaspoonful of human serum was flown from California to Connecticut for a test and confirmed the diagnosis of overactive thyroid more quickly than routine methods on the scene, in San Francisco.

"March of Death" Cases

Such tests are also used to control the treatment in specific cases, so as to make sure of the right dosage. Among cases treated and controlled by these methods were those of certain men who were victims of the "March of Death" at Corregidor, Philippine Islands, during the war. As a result of malnutrition, some of these men developed breasts like women and tests showed that starvation had reduced their production of normal male hormones. Similar findings have been made in cases of people suffering from liver disease.

In women, these tests are helping to trace the cyclic changes in sex hormone secretion leading up to ovulation and during pregnancy.

Locating Tumor in Surgery

Radiophosphorus is being used at Harvard Medical School to locate brain tumors during surgery. Experiments showed that brain tumors, following intravenous injection, absorbed many times as much phosphorus as the normal brain tissue—in some cases over 100 times as much. The rays emitted by the radiophosphorus, however, penetrate only a little more than one-quarter of an inch through brain tissue. Thus, in locating the tumor, it was necessary to have a counter small enough to be inserted into the brain during surgery. Such an instrument was being devised in the Physics Department of the University of Wisconsin, and it was almost ready for use at the time that the technique was first hit upon.

The combination of radiophosphorus injection and this tiny counter, has been used successfully in 14 operations to remove brain tumors.

Isotopes in Treatment

Radioactive iodine has been used in the treatment of Graves' disease (exophthalmic goiter) in which the thyroid gland is overactive. There are other means of treatment in these cases, including surgery to remove the gland. Radioiodine treatment is effective because the iodine

has an affinity for thyroid tissue and the radioactive isotope, deposited in the gland, depresses its activity by the effect of the radiation. It is often useful where surgery has been unsuccessful and the gland has recurred after operation. Studies supported by the Commission at the Memorial Hospital, Yale University, University of California and the Columbia University College of Physicians and Surgeons have verified this means of treatment.

Easing Heart Pains

Radioactive iodine also is being used at Harvard University to relieve pain and distress in two types of heart disease—angina pectoris and congestive heart failure. Previous studies showed that lessening of thyroid activity would so diminish the body's demands upon the heart as to reduce markedly the choking sensations and pain of angina pectoris and the shortness of breath and dropsy of congestive heart failure. Useful in a small percentage of cases that do not yield to other therapy, treatment to reduce the activity of the thyroid by use of radioiodine has been tried on 19 patients. In five of nine suffering from angina pectoris, the pain was strikingly lessened or abolished and several are now gainfully employed. In four of seven patients with congestive heart failure, shortness of breath has been alleviated and ability to work increased. When thyroid deficiency is too marked, small dosages of thyroid substance improved the condition of patients. This treatment still needs further investigation.

C. CANCER PROGRAM

The Commission is expanding its part in the Nation-wide quest for knowledge about cancer and for means of controlling the disease. Recently, the Commission has taken the following steps:

(*a*) Approved plans for the 50-bed Argonne Cancer Research Hospital and for a 32-bed clinical cancer research hospital at Oak Ridge.

(*b*) Supplied all radioisotopes now being sold to qualified cancer research workers in the United States without production charges.

(*c*) Sponsored research, and provided radioisotopes, to determine the efficiency of radiocobalt (cobalt 60) as a substitute for radium in the treatment of cancer.

The Commission also is continuing its support of a score of research projects inquiring into the causes of cancer, the nature and metabolism of cancer cells, their effect upon body processes, and various devices for diagnosis and treatment.

Cancer Research Facilities

Although animal experimentation in the cancer field is of considerable value, there is also a need for studies on human beings who are suffering from the disease. For this part of its cancer program, the Commission is financing two cancer research facilities. The first of these, the Oak Ridge Cancer Hospital, to include 32 beds in the Oak Ridge Hospital, is being developed by the Oak Ridge Institute of Nuclear Studies. In addition, appropriate laboratory facilities will be erected. This facility will be operated by the deans of the southern medical schools affiliated with the Oak Ridge Institute. It is anticipated that a number of short-lived radioactive isotopes which are obtainable from the reactor at Oak Ridge will be studied for their application in the cancer field.

The Argonne Cancer Research Hospital is intended primarily for research in which radioisotopes will be used to treat cancer patients. The hospital will be operated by the University of Chicago for the use of medical schools affiliated with Argonne. The structure, to cover some 100,000 square feet and cost about $3.5 million is scheduled for use in 1951. Only two of the six floors will be reserved for patients, and the rest will be devoted to laboratories, offices, electronic, and radiology shops.

Patients for the new hospital will be carefully selected so that new types of treatment can be given a thorough test under the very best of conditions. Much auxiliary research will be carried out.

Besides providing the hospital and the assistance of its trained staff, the Argonne National Laboratory will:

(*a*) Produce radioisotopes in its nuclear reactor for the hospital. Since it is nearby, only 25 miles southwest of Chicago, Argonne can supply the hospital with short-lived isotopes that otherwise could not be used.

(*b*) Assist in synthesizing radioactive materials into medically useful compounds and drugs.

The hospital will provide a clinical proving ground for scientists of Argonne National Laboratory and its 31 participating universities, colleges and research institutions.

Isotopes For Cancer Research

The Commission has set aside $450,000 to supply radioisotopes—free except for handling and shipping charges—to qualified cancer research men in the United States during the year begun last March. This sum will cover production costs of the isotopes of 50 additional elements now added to the three originally supplied on this basis.

The list includes all radioisotopes now being sold by the Commission. Notable among these are radiogold, radiocarbon, and radiocobalt. Cobalt 60 has promise as a substitute for the rare and expensive radium used for years in cancer research and treatment.

Charges made to the research institutions include actual transportation charges, plus $10 for packaging, monitoring, accounting, and billing. When the Commission laboratory synthesizes a compound, the user will be billed for this work but not for the isotopes in the compound.

Under this plan, isotopes will be allocated for (*a*) cancer research in animals, (*b*) research on the basic metabolism of cancer cells, and (*c*) programs experimenting in treatment of cancer. Resale or charges to patients for isotopes received under this program are forbidden and a proposal for use of the isotopes for patients must be approved by the Subcommittee on Human Applications, of the Commission's Committee on Isotope Distribution. The Committee, composed of leading physicians, has set up the following restrictions:

(*a*) The attending physicians must be associated with an organization that possesses adequate radioisotope facilities.

(*b*) The organization's isotope committee must approve the intended use.

(*c*) The physician must be in good standing with the local medical society and either have previous experience with radiation or be collaborating directly with those who have.

Radiocobalt and Cancer

The value of radiocobalt in cancer research and treatment is being determined. In treatment, radiocobalt is used as a substitute for radium which is one of the established tools for destroying cancer cells.

Radiocobalt gives off radiation that is very much the same as that of radium in its effects, but a milligram of cobalt 60 will produce less radiation than the same amount of radium. Scientists have evaluated this difference between the two elements on a theoretical and experi-

mental basis. Their findings have made it possible to try out special techniques for the use and handling of radiocobalt to test its worth in treating cancer.

In certain types of applicators for cancer treatment, radiocobalt has a positive advantage over radium. In using radium, physicians typically may imbed it in a wax form modeled to fit the inside of the mouth, the outside of the jaw, or the cervix. The pattern in which radioactive seeds are placed in the form is extremely important. The radiologist tries to meter the dosage, by his placing of the seeds, so that cancerous areas receive the correct radiation and so that the applicator will create no "hot spots" to cause serious local over-exposure.

Radiocobalt vs. radium. Difficulties arise in such treatments with radium both because of its cost and the fact that radium is usually contained in nonpliable tubes. On the other hand, radiocobalt is relatively cheap to produce and can be used in any reasonable quantities. It can be made up in various pliable shapes with different rates of radioactivity. These factors combine to make it easier to distribute properly in such a wax form.

Another advantage of cobalt is that it can be prefabricated in an ordinary laboratory before it is irradiated. Even after being made radioactive, it can be stored with proper protection as a fine wire on a spool and clipped off in desired quantities as needed. It also can be made in an alloy form with nickel to improve its metallurgical properties.

Where costs are concerned, the price of radium is between $15,000 and $20,000 a gram, whereas radiocobalt can be had at a minimal charge for handling. However, radium is, for all practical purposes, of permanent value to an institution, since it requires 1,500 years to lose half its radioactive strength. By contrast, radiocobalt has a half-life of 5 years. This comparatively rapid decay also makes it necessary to measure the radiation of a quantity of cobalt 60 before application.

From another viewpoint, radiocobalt has a further advantage. Radium is very dangerous if accidentally set free in the body, since it remains in the body and continues to destroy tissue for many years. Cobalt, on the other hand, is rapidly excreted.

Protection similar. In general, any medical institution properly staffed and equipped to handle radium is in an excellent position to make use of radioactive cobalt. Radiologists do not believe that radiocobalt should be used by institutions not fully qualified for radium handling since the cobalt, like radium, can be dangerous. Precautions should be essentially the same for both materials. Cobalt, however, does have two additional advantages. It is magnetic and

consequently may be handled with electromagnetic holders at some distance from the hands or body so as to reduce exposure to its radiations. Moreover, the energy of beta particles emitted by cobalt is considerably less than that of the alpha particles from radium, and this simplifies the shielding problem substantially.

The Commission, in addition to providing radiocobalt to research institutions without charge for cost of production, sells the element at a cost substantially less than that of radium for treatment of paying patients.

Research Using Radiocobalt

Exposure of animals to radiocobalt radiation at Ohio State University indicated that the effects were similar, if not identical, to those expected from other radiation sources such as radium. Methods of safe handling were developed so that applicators could be used on human patients without excessive exposure of the technical staff to radiation.

In limited usage, during the last 9 months, cases were treated which otherwise could not have been successfully irradiated with the means at the university's disposal. Where a cancer-killing dosage was administered, the tumor died. In some cases, only temporary arrest of the disease could be expected because of the amount and area involved, but the arrest was accomplished. About 15 cases of 5 general types of cancer have been treated and no untoward effects observed.

Indications are that, due to the flexibility and comparative safety of radiocobalt, the university will be able to achieve its original objective of better treatment of cancer. Evaluation of results will require further large scale work and some years of time.

Use of activation analysis (see p. 494) by the University of California Radiation Laboratory showed that the amount of cobalt distributed in the entire human body is about a half microgram—a mere trace. It enters the nucleus of certain tissue cells and, normally, the half-life time of its loss from the body is about one day. However, in mice with cancer of the breast, approximately twice the normal amount of cobalt was taken up by liver cells and, at a somewhat later time, appeared in the nuclei of cancer cells.

Research chamber. A radiation exposure chamber, using cobalt 60 as a source of rays to test their effect upon laboratory animals, is nearing completion at the University of Illinois. The cell, using about 6 curies of cobalt 60—each curie having about the same number of atomic disintegrations as a gram of radium, or a total of some 222 billion disintegrations per second—can administer very low to fairly

high dosages to mice. It cannot handle any animal larger than a rat but will be capable of 4,500 roentgen units of radiation per hour—some nine times the estimated lethal dosage for man.

The exposure chamber is an important instrument for testing radiation effects upon living animals and will add to an understanding of cobalt 60 in cancer treatment. The degree of radiation injury is conditioned by both the intensity of the rays and the duration of exposure. Thus, 500 roentgen is considered a lethal dosage of radiation if administered within an hour, but if the same amount of radiation were stretched out over a longer time its effect would be less serious. It is possible that if 500 roentgen of radiation were scattered over a long enough time, about 5,000 hours, that it would cause almost no injury.

The University of Illinois experiment, besides testing the radiation effects, will assist in designing applicators to fit particular needs in cancer therapy.

Cancer Research Projects

Cancer research, sponsored by the Commission, has a dual purpose. It seeks to learn the basic structure and processes of cells—for cancer is preeminently a disease of the cell—and methods of using radioisotopes to diagnose cancer and to destroy tumors. It has the further purpose of studying radiation effects in man since in cancer patients heavy irradiation can be studied more intensively and with greater justification than under any other circumstances short of war and accidents.

A great deal of basic research is essential to a solution of the cancer problem. In trying to understand the subtleties of cancer cell behavior, we must have a firm understanding of the normal cells.

Nucleic Acid as a Key

Knowledge of the details of nucleic acid metabolism should provide better means for combating, for measuring, and for enhancing the effects of radiation.

The simpler organic components that enter into the formation of nucleic acid have been prepared in the laboratory at Memorial Hospital, Sloan-Kettering Institute, and labeled with isotopes. Radiocarbon (C 14) has been used, and the nonradioactive heavy isotopes of nitrogen and carbon. These components are then fed to animals to ascertain which compounds in what amounts go to normal cells as well as to cancerous tissue.

One artificial compound has been prepared which, in mice, has a temporary controlling effect upon leukemia. This substance enters into the formation of a product of cell decomposition called guanine. Its effects on man have not been fully explored, but this particular compound probably is not effective in control of cancer. Numbers of related compounds have been formed (the compound itself is 2,6-diaminopurine) and they are being tested. Some have a controlling, but not curative, effect on some forms of animal cancer. It is also possible that compounds of this sort may be found to protect against, or to relieve, radiation injury.

Proteins in Cancer

No tissue can grow without increasing its mass of protein, which is incorporated into cell structure. Control over growth, as in a cancer tumor, requires an understanding of this continuous process of building up and breaking down proteins. In normal, nongrowing tissue, the process is in delicate balance. In cancer, the building process is excessive. A considerable amount is known about the enzymes that break down proteins, but little, until recently, about the opposite process.

At Huntington Memorial Hospital, tissue slices were incubated with radiocarbon—tagged amino acids—the basic stuff of which proteins are formed. The acids were taken up in the protein of the tissues, but it was found that two factors would stop the process: the absence of oxygen, or the addition of minute amounts of dinitrophenol—a drug known to prevent the formation of energy-rich phosphate bonds, once used clinically to help in weight reduction. Slices of tissue from the cancerous livers of rats take up one of the amino acids—alanine—six times as fast as normal liver.

Radiation As a Cause of Cancer

Radiation can cause cancer as well as control it, and this effect requires full study. A great number of experiments undertaken at Argonne, Oak Ridge, and the National Cancer Institute, to determine what levels of radioactive rays and isotopes may be considered safe for workers in the atomic energy field, have been useful in helping to understand how cancer arises. Argonne is trying to discover whether radiation produces cancer by chemical or other types of injury to the cell.

Experimenters are irradiating normal chemicals of the body to find whether they form cancer-producing chemicals. They are separating out microscopic parts of cells and using the electron microscope to

look for changes caused in them by radiation. One puzzling question is the considerable time which elapses between radiation and the appearance of cancer. Tissues and cells are being examined carefully for chemical and structural changes which must occur during this period, but which are invisible by ordinary means of examination. For example, the changes in the lens of the eye resulting from neutron exposure might be missed in tissues, such as muscle, which are not transparent. Low-level radiation is being studied by subjecting normal body chemicals and cells to neutrons from the nuclear reactors.

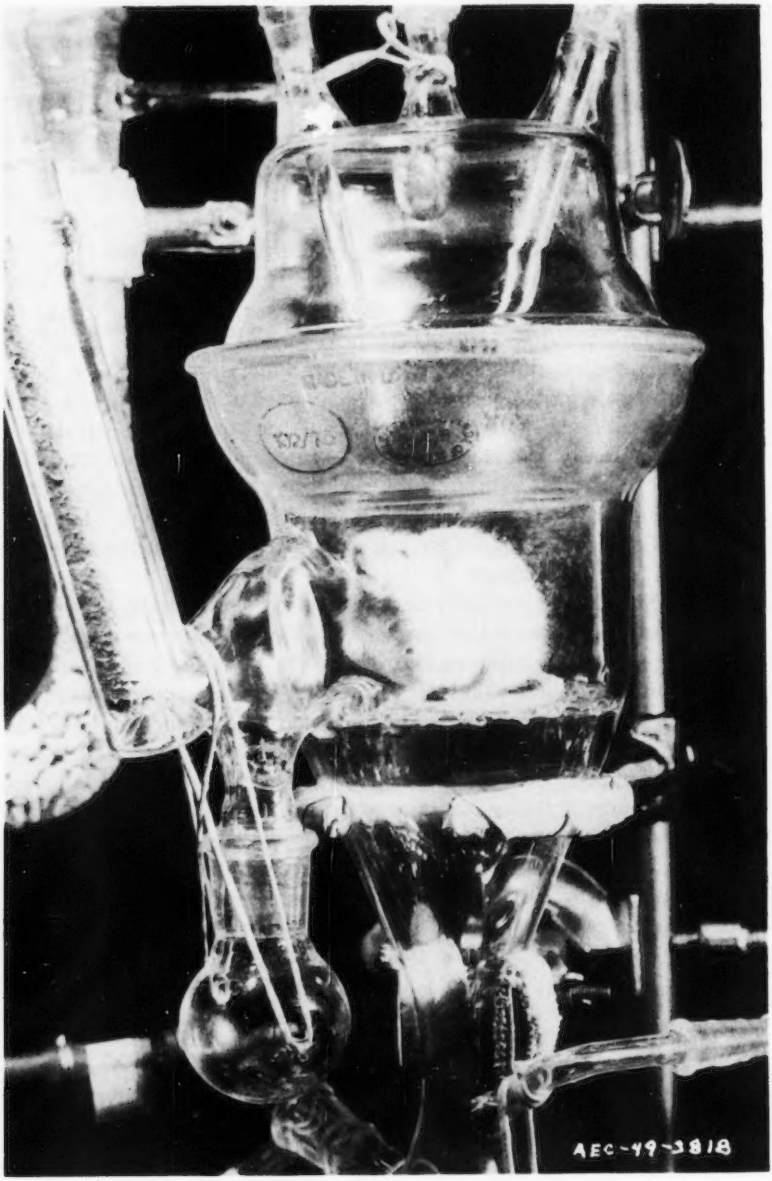
The way in which the metal beryllium, now coming into larger industrial uses, causes cancer of the bone was studied by injecting beryllium into rabbits at Huntington Memorial Hospital. A group of enzymes, called phosphatases and extremely important to bone growth, are normally accelerated by magnesium—an element that closely resembles beryllium. Beryllium, on the other hand, inhibits the action of the enzymes. The experiments suggest that the enzyme is "fooled" into taking on beryllium instead of magnesium, and then is prevented from performing its normal function. Further studies will seek to clarify the relationship of these two elements and of calcium to other enzymes.

Other experiments are directed toward learning more about the effects of some isotopes which can be valuable in treatment of disease, but which are also dangerous because of the way in which the body stores them. The best example of such an isotope, potentially both dangerous and of enormous value is carbon 14. Since the half-life of this carbon is about 5,000 years, its prolonged retention in the body might cause cancer.

The tolerance of living organisms for the radiation effects of various compounds of radiocarbon is being investigated at Argonne, Southern Research Institute, and the Universities of Minnesota and California. Carbon enters into all the organs and tissue of the body and is a prime research tool, but research using radiocarbon is limited at present to animals. In the case of radioactive sodium bicarbonate, or of inhaled carbon dioxide gas, it has been learned that the radiation hazard is probably not as great as had been expected. Workers at Southern Research Institute are looking for other forms in which radiocarbon may be used in human patients and have combined it into urea, ethyl alcohol, and urethane, substances of interest in cancer study.

Isotope Treatment of Cancer

In using radioactive isotopes to treat cancer, physicians seek to destroy the growth by placing a source of radiation within the malig-



Laboratory mice, after taking food "tagged" with radioactive carbon at Los Alamos laboratory, are placed in all-glass metabolism cages which collect exhaled air and other body excretions. By following the tagged carbon, scientists learn new facts about the workings of the body, of man as well as the mouse.

nant cells themselves. If they can concentrate the radiation in this way with high efficiency, the patient will suffer less general radiation exposure than from typical treatment by X-ray or radium. High efficiency is possible only if a tumor readily and rapidly absorbs the radioisotope, and if the rest of the patient's body takes up only harmless amounts.

Cancers vary widely in type. One tumor may absorb a radioisotope of one type with avidity, another may not take it up at all. So far, physicians have been most successful in using radioiodine to treat cancers of the thyroid.

Facts About Radioiodine Treatment

Use of radioiodine to treat patients with thyroid cancer at the Sloan-Kettering Institute, Memorial Hospital, has developed the following facts:

(*a*) Each patient requires careful study since absorption of iodine by a specific thyroid cancer depends upon the nature of its tissues and varies with each case.

(*b*) Irradiation damage from radioiodine deposited in or near specific cells differs from that caused by the same amount of radiation more generally distributed.

(*c*) Thyroid cancer that shows no affinity for radioiodine can be caused to take up large amounts of isotopes by procedures developed through research. This fact is of utmost importance in treatment, but it further establishes that cancer is not a wholly separate growth, independent of all control. It indicates that cancer may respond to stimuli of the parent tissue from which it arose. It suggests further that other forms of cancer may be caused to absorb materials.

(*d*) Extensive destruction of certain thyroid cancers can be achieved by radioiodine therapy administered under certain circumstances. It is not clear that cancer can be entirely cured. More work is urgently needed.

(*e*) Individual patients react in very different ways to the radiation of radioiodine when it is injected into the system.

Similar studies in use of radioiodine are under way at Harvard and Yale Universities, at the University of Chicago, and at other medical centers.

"Guiding" Radioisotopes to Cells

As indicated, radioiodine has definite advantages in treating cancer, but its use is sharply limited because normally it goes almost exclusively to the thyroid gland, or to cancers that have spread from this source. Scientists are attempting to direct radioiodine, and other isotopes such as radiosulfur, to other possible sites of cancer in the body. They do this by attaching the radioisotope to a "guide" that when injected into the system will go, for example, to the kidney. Research men prepared the "guide" by injecting mouse kidney tissue into a rat, then extracting from the rat the antibody which it built up to resist this alien material. When this antibody is placed in a solution of the radioisotope, it will absorb a quantity of the radioactive material. Injected then into a mouse, the antibody "guided" large amounts of the isotope to the kidney with extraordinary speed. Guides have been similarly prepared which will carry radioiodine to the lung and this establishes that the principle of using a guide is not confined to a single tissue. Scientists at Sloan-Kettering hope similar guides may be prepared to carry radioisotopes to cancer tissue.

A compound, stilbamidine, known to localize in myeloma cells—cancerous cells of the bone marrow—has been synthesized with radiocarbon at the Radiation Laboratory, University of California. Since this type of cancer occurs only in humans, the use of this substance to guide radioactive material to cancer cells is awaiting clinical tests.

Other Isotope Treatment

Radiophosphorus is now a standard treatment for certain blood disorders. Its use at New England Deaconess Hospital, Western Reserve, University of California, Berkeley, and many other hospitals to treat leukemia and polycythemia indicates that most cases of polycythemia vera can be controlled by dosages of 2.5 to 5 millicurie of radiophosphorus as disodium phosphate, either by injection or by mouth. Cases of leukemia that have become resistant to X-ray treatment may be helped.

Experiments in embryo chickens to test the effect of this form of treatment on the bone marrow and other tissues indicates dosages much heavier than used in treatment were required to produce damage.

Radiophosphorus is absorbed by stomach tumors in human patients much more rapidly than by normal tissue, tests at Harvard University and Peter Bent Brigham Hospital showed. There was an increase of 124 percent in the turn-over of protein phosphorus in stomach cancer. The effects of stomach secretions on this process are being

studied. The rapid absorption of protein phosphorus by other tumors such as those of the skin, has been studied at the University of California Medical School.

Colloids. Methods of placing radioactive materials in the lymphatic system of the body, a medium through which cancer frequently spreads, have been devised at the Radiation Laboratory, University of California. Certain yttrium colloids, injected into a lymphatic vessel, spread uniformly through the network of lymph nodes above the injection. Patients with cancer will be treated experimentally by this method.

Radioarsenic. Physicians at the University of Chicago and Argonne Laboratory have been testing the value of radioactive arsenic in treating blood diseases and cancer. Nonradioactive arsenic is a useful drug in leukemia. It can be made radioactive by irradiation in the nuclear reactor, should it turn out that its value in treatment is increased by radioactivity. This is but another example of the host of radioactive agents which must be studied in an effort to discover new forms of treatment.

D. RADIATION AND AGRICULTURE

Parallel to efforts to use radiation and radioisotopes for the direct medical benefit of mankind, the atomic energy program is aiding in some of the Nation's research which adds to basic knowledge of the effects of radiation on food-producing plants and animals. Typical among projects sponsored by the Commission are: (*a*) a study, at University of Tennessee of the effects of radiation upon cattle exposed to radioactive dust outfall from the Alamogordo (N. Mex.) bomb test; (*b*) widespread studies managed by the Department of Agriculture on the effects of radioactive fertilizer on growth of plants; (*c*) studies by the Department of Agriculture directed toward understanding how fertilizers feed into plants and determining the most favorable cycles of fertilizer application; and (*d*) an extensive group of projects dealing with such diverse subjects as studies on photosynthesis of plants; mineral nutrition of plants and domestic animals; use of radioactive materials as tracers to study action of fungicides and herbicides; the action of radioactive materials on disease-producing fungi; and the possibilities of using radioisotopes for therapy in plant diseases.

Domestic Livestock

The University of Tennessee, Knoxville, has contracted with the Commission to study the effects of radiation upon domestic and laboratory animals.

Facilities to carry out this rather extensive research program will be completed during the fiscal year 1950: (*a*) about 1,000 acres of improved farm land will be used for the maintenance of cattle exposed to the "outfall" of radioactive materials at Alamogordo, for farm animals to be used in tests, for facilities for pilot-scale trials of practical findings, and for any emergency studies which may be required; (*b*) laboratories will be completed for metabolism studies for animals ranging in size from mice to mature cattle. These will include "hot" rooms, a nutrition barn, two radioassay laboratories, radioactive counting rooms, two biochemistry laboratories, a small animal room, a darkroom, and supporting facilities.

The herd of cattle inadvertently exposed at Alamogordo included calves, yearlings, steers, cows, and bulls. Of the 26 cows and 24 heifer calves, 43 are still living. Seven died from causes which could not definitely be attributed to their exposure.

Forty-nine of the 50 cows have produced calves, all of which were normal. A total of 57 calves have been produced and 48 are on hand. One of the exposed bulls was bred to exposed cows and from these matings 33 normal calves were produced. There is no evidence up to date of any adverse effects on the fertility of either the exposed cows or bulls.

Several steers will be autopsied and studied for radioactivity and radiation injury. Experiments will be made to evaluate any possible health hazard from eating the meat of such animals.

Other cattle exposed to some radiation at the time of the Alamogordo bomb test will be observed over their life span. Breeding records will be kept and abnormalities noted. Studies will be made each six months to reveal any prolonged changes that may occur. (See photograph, opposite.)

Radioactive Fertilizer Tests

Since the discovery of radioactivity, claims have been made that radioactive substances stimulate plant growth. Early and nontechnical reports from Japan indicated greatly enhanced crop yields in the vicinity of the bombed areas. Although scientists refuted these claims, interest in the use of radioactive materials to improve crop yields has continued. Many experiments have been conducted over the past 30 or 40 years in this country and in Europe to measure the effects of radia-

Range cattle inadvertently exposed to radioactive dust in first atom bomb explosion in New Mexico, 1945, to be studied along with their offspring at University of Tennessee for possible effects. Gray hair, shown, was only effect immediately observable.

tion. Because experiments were not conducted in adequate numbers under carefully controlled conditions, results have been conflicting and inconclusive. Some observers noted beneficial effects, others no effects, and still others harmful effects.

Under a contract from the Atomic Energy Commission to determine whether radioactive material does indeed stimulate plant growth, the United States Department of Agriculture undertook a project in cooperation with the State agricultural experiment stations of Arkansas, Florida, Illinois, Kentucky, Michigan, Mississippi, Montana, New York, North Carolina, Ohio, Washington, West Virginia, and Georgia. One of the first aims was to ascertain whether a farmer or gardener could significantly increase crop yield by adding to the soil one of several naturally radioactive materials.

Radio Materials and Crops Used

Three radioactive materials were used in the field experiments in 1948: radium, uranium, and a commercial material said by the manufacturer to derive its radioactivity principally from actinium. Radium was used at the rate of 300 micrograms per acre, uranium at a comparable level of alpha radiation. The commercial material was applied at one-half and double this rate in terms of alpha disintegrations.

Carefully replicated experiments were conducted with the following crops:

Corn	Illinois, Mississippi, and West Virginia
Wheat	North Dakota and Washington
Barley	North Dakota
Oats	Illinois
Soybeans	Illinois (2 locations)
Beans	Michigan and Washington
Sugar Beets	Washington
Table Beets	Michigan
Turnips	Maryland
Carrots	New York and Florida
Potatoes	Montana and New York (2 locations)
Sweetpotatoes	Arkansas (2 locations)
Spinach	Michigan
Tomatoes	Maryland and Kentucky
Cotton	Georgia (2 locations)
Tobacco	North Carolina
Peanuts	North Carolina

Research Reveals No Benefits

These experiments revealed neither benefits nor damage to crop growth and yields from the radioactive materials applied.

The conclusion is that there was no measurable effect at the levels of radiation used. Tests are being continued this year to observe possible second season effects on the same plots of land. Additional experiments are being conducted in the greenhouse to determine the effect of radium and uranium, over a much wider range of concentration than used in the field experiments, on the growth of vegetable and floral crops. So far no beneficial effects have been observed.

Radiation Effects on Crops

At Brookhaven laboratory, the effect on plants of continuous exposure to gamma radiation from a 20-curie source of cobalt 60 is being studied under field conditions. Corn, tomatoes, potatoes, spider wort, and a number of cultivated species are being exposed during the whole growing season at a wide range of radiation intensity. Scientists hope to obtain valuable information on gene and chromosome mutation rates and on general effects on growth, yield, and resistance to infection. (See photograph, on following page.)

Isotopes in Agricultural Research

Improved use of fertilizers for crops depends upon a better understanding of the fate of fertilizers placed in the soil, and of the movement into plants of the nutrients that they supply. Radioisotopes offer, for the first time, a tool by which these facts can be discovered accurately and in detail.

However, extensive study of fertilizers by these means depends upon developing safe techniques for handling long-lived isotopes and others that may be poisonous to man. A group to study these problems is now being organized in the Bureau of Plant Industry, Soils and Agricultural Engineering at Beltsville, Md.

Experiments during 1947 and 1948 by the Bureau, in cooperation with State experiment stations of North Carolina, Iowa, and Colorado, indicated that radiophosphorus can be used efficiently in studying fertilizer problems. Success of these initial projects has led to widespread demand for similar work on diverse soils, crops, climates, and fertilizers. To meet this demand, the Bureau built a small scale fertilizer plant to introduce radiophosphorus into six principal types of phosphatic fertilizer for experiments by 12 State organizations. To guard against danger in field work from the radioactive dust, it perfected an endless belt type of distributor.

State Fertilizer Research

State agricultural experiment stations, using these fertilizers in cooperation with the Department of Agriculture are conducting ex-

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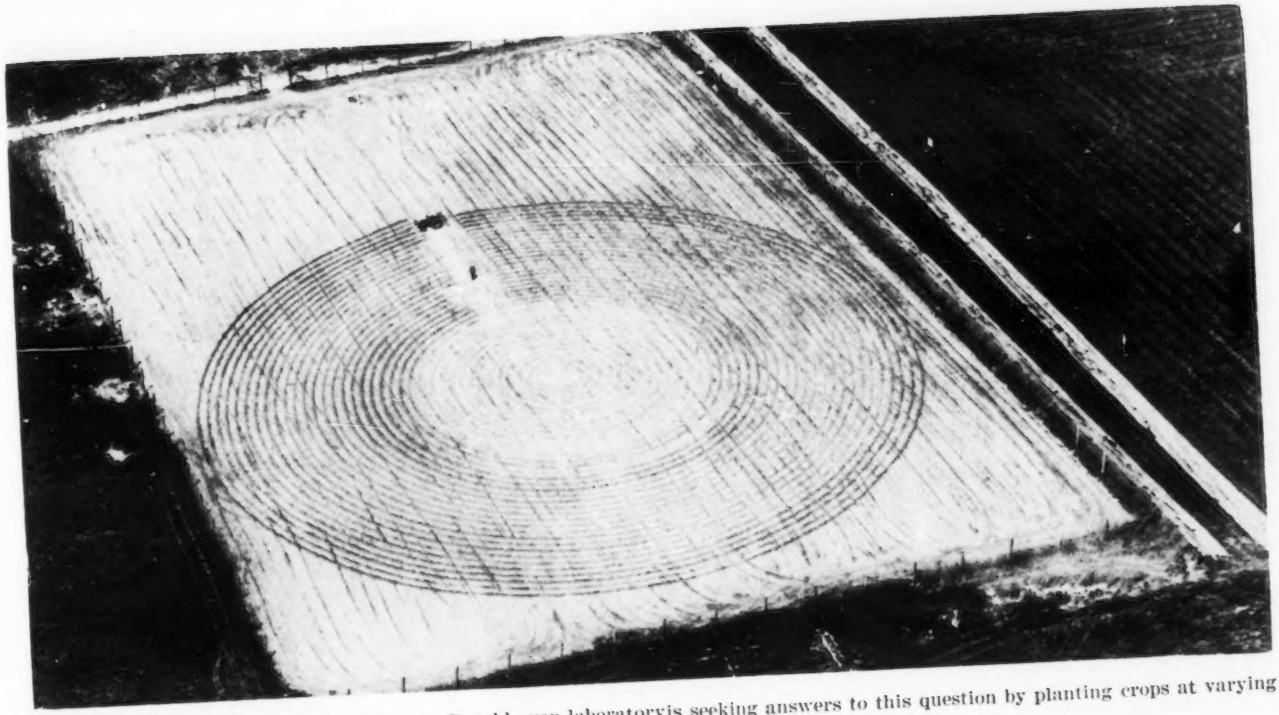

How does radiation affect growing plants? Brookhaven laboratoryis seeking answers to this question by planting crops at varying distances from a source of radiation (radiocobalt) to be placed on the pole, center.

periments which deal with the peculiarities of crop demands, effectiveness of various placement of fertilizers, plant response to different rates of application, and the absorption by several crops on different soils of different fertilizer materials. Thirty-five separate cooperative experiments are being run during 1949.

Under contract with the Commission, fundamental studies with radioisotopes at North Carolina State College are being conducted on the movement of chemical ions in the soil. This research will give a better understanding of the chemistry of some of the clay soils of the South.

At the University of Missouri, plants were grown in sand and then transferred to water in which radiophosphorus was placed so as to pattern the movement of the mineral through the plant. Young leaves or leaves that resume growth, it was found, accumulate the phosphorus most rapidly, and even drain it from storage in other parts of the plant. The scientists devised a shielded instrument which could be attached to plant leaves to measure radioactivity without damaging the leaves. The experimenters will next study calcium distribution.

Studies on How Plants Grow

At Brookhaven, Oak Ridge, and Argonne National Laboratories, and at the University of California, radiocarbon is used to study how plants manufacture sugar with the aid of the sunlight from carbon dioxide and water. Plants are used to manufacture radioactive sugar for use in other experiments. The process is to place the plant in the dark until it has used up most of its own sugars and then to expose it to sunlight in a container filled with radioactive carbon dioxide. Scientists are also investigating the mechanics of this process in the hope of some day being able to perform the same process artificially outside of plants.

Investigating Plant Diseases

Radioisotopes are being used in research on plant diseases. At the University of Minnesota, scientists are studying fungi that cause plant diseases by growing them in a substance that contains radioactive materials. They are seeking to gain a better understanding of the great variability in races and strains shown by these parasites, which are similar to the black stem rust that destroys wheat, to ergot in rye, and to smut that affects corn. In the history of breeding for resistance to disease, many instances are known where varieties formerly recognized as resistant have later been attacked by the development or introduction of new and more violent strains of smut. Any under-

How plants grow and make use of nutrient material is being studied with radioisotope tracers by U. S. Department of Agriculture. Above, research worker checks radiation from "tagged" fertilizer added to soil; below, plants are dissected to find how radioactive material has been distributed in leaves, stems, roots, and other parts during growth.

standing of how the great number of races and strains of smut are generated, and of their mechanics, may aid in overcoming this costly menace.

University of Ohio is studying the effects of radiophosphorus on several such fungi, and testing the feasibility of "tagging" spores with radioactive material so that the spread of plant diseases can be traced. Scientists who have specialized in using chemicals to treat plant diseases are testing whether radioactive materials will help in controlling the diseases. At Battelle Memorial Institute, plant experts are using radioisotopes to trace the effects of fungicides in destroying parasitic fungi.

In the foregoing pages, only a few research contracts dealing with agriculture are described in detail. In addition, both in the laboratories of the Commission and through support of research contracts in universities and other institutions, the Commission is assisting the Nation's widespread agricultural research with radioactive materials. Commission projects which include those dealing with genetics and particularly with genetics on such commercial crops as peanuts, Irish potatoes, corn (see p. 465), and tomatoes have a direct application in agriculture. Some of these projects are mentioned in other portions of this report, and all of those being carried on through direct contract with universities and colleges are listed under "Biology and Medicine Research Contracts."

4. DEVELOPMENT OF THE PROGRAM

Even so condensed a report as the foregoing makes clear how great is the impact of atomic energy upon the life sciences: how it opens new vistas of better health, of more abundant food supply, of greater control by man over his environment; and how—along with its promised benefits—it has created new potential dangers for its discoverers and their descendants. This report also emphasizes that the achievement of these benefits and the avoidance of these dangers both depend upon the acquisition of new knowledge—upon the full explanation of a great number of biological and medical processes within a relatively short period of time.

In writing the Atomic Energy Act of 1946, the Congress recognized that this advance in knowledge, if it were to be sufficiently rapid, called for Federal assistance. It directed the newly established Atomic Energy Commission:

> to exercise its powers in such manner as to insure the continued conduct of research and development activities . . . . by private or public institutions or persons . . . and through its own facilities . . . and to assist in the acquisition of an ever-expanding fund of theoretical and practical knowledge in . . . . utilization of fissionable and radioactive materials for medical, biological, health, or military purposes . . . . and the protection of health during research and production activities.

For planning its course of action under this broad charter, the Commission sought the guidance of recognized leaders in the field of biology and medicine in the United States. After taking office in 1947, it appointed a Medical Board of Review from a panel of scientists and educators nominated by the President of the National Academy of Sciences. In June 1947, this board submitted a report which has had an important influence on the development of the Commission's program.

The board based its recommendations upon two broad propositions: first, that there was an extremely urgent need for expansion of research in the effects of atomic energy upon biology and medicine and for training of many more scientists in this field; and, second, that the Commission was the organization with primary responsibility on a national scale, to see that this research and training was done—not alone because of its statutory obligation laid down in the Act, but also because it was the agency holding the monopoly—sometimes partial and sometimes complete—over the production of atomic energy materials, the handling of such materials, the technical processes, and the war-developed scientific and technical information. Specifically, the board recommended that the Commission:

(*a*) Expand research on the biological effects of radiation on a Nation-wide scale—in its own installations and also in universities and other outside institutions whenever the nature of the work permitted.

(*b*) Take primary responsibility for the protection of health against atomic energy hazards—conducting studies and training personnel in its own installations and making use of the assistance of outside institutions whenever feasible.

(*c*) Continue to distribute isotopes at nominal prices for research in all the sciences; provide assistance in their safe utilization; and consider making them available to foreign investigators.

(*d*) Actively encourage the circulation of scientific information, the declassification and publication of the scientific papers produced by the atomic energy project.

(*e*) Work closely with the medical personnel of the Armed Forces and with the United States Public Health Service to develop the knowledge, the techniques, and the trained personnel needed to protect Americans from the hazards of atomic energy in peace or war.

(*f*) Institute a fellowship program to train promising students for careers in the field of the biological and medical effects of radiation; also, a technical training program in the techniques and skills of "health physics."

(*g*) Aggressively survey the human resources of the Nation for the task ahead: (*i*) the centers of teaching and other sources of recruitment of the great number of additional workers needed, and (*ii*) the workers already in the field, who would necessarily be key figures in the expanding program.

(*h*) Create a permanent Advisory Committee for Biology and Medicine, to recommend to the Commission a general policy of research and health; and, finally,

(*i*) Appoint within the Commission a medical director to assume general responsibility for the research and training programs in both biology and medicine and for health protection activities.

Every one of these recommendations has been turned into a going program during the 2 years since they were made.

Advisory Committee for Biology and Medicine

In September 1947, the Commission appointed a permanent Advisory Committee for Biology and Medicine, of the following distinguished leaders in the field, all of whom are still serving at this time:

Dr. Alan Gregg, director for medical sciences, Rockefeller Foundation, New York, N. Y., chairman.

Dr. Ernest W. Goodpasture, dean of the school of medicine and professor of pathology, Vanderbilt University, Nashville, Tenn., vice chairman.

Dr. G. W. Beadle, chairman of division of biology, California Institute of Technology, Pasadena, Calif.

Dr. Detlev W. Bronk, president, Johns Hopkins University, Baltimore, Md., and chairman, National Research Council.

Dr. A. Baird Hastings, professor of biochemistry, Harvard Medical School, Boston, Mass.

Dr. E. C. Stakman, chief, division of plant pathology and botany, University of Minnesota, Minneapolis, Minn., and President, American Association for Advancement of Science.

Dr. Joseph T. Wearn, dean of the school of medicine, Western Reserve University, Cleveland, Ohio.

The Commission has depended heavily upon the wisdom and experience of these men for the development of its program. They have devoted their time and energies to this task to an extent far beyond the usual participation of advisory bodies. They have met 16 times within the past 2 years and have become thoroughly acquainted with every phase of the national atomic energy enterprise.

A look at the agenda of a recent meeting of the Committee reveals how extensive and intensive is its participation in the Commission's work. Meeting at Los Alamos, the Committee reviewed research projects that had been proposed for AEC support by various universities and recommended acceptance, rejection, or further consideration in each case; discussed the problem of how best to handle the radiation-exposure history of AEC employees when they change jobs or leave the project; proposed methods of publicizing the fellowship program among young scientists; reviewed the program of Los Alamos laboratory, the need of a long-term program, the need of tenure for scientific workers, and the construction of a hospital; considered the adequacy of the fencing around Alamogordo bomb explosion site; gave advice on certain technical aspects of the disposal of radioactive gases; advised against the creation at this time of a fourth AEC "national laboratory"—all this in addition to making a thorough inspection and evaluation of the biological and medical program at Los Alamos.

AEC Division of Biology and Medicine

One of the first services of the Committee was to assist the Commission in establishing in its Washington headquarters a Division of Biology and Medicine and in recruiting the experienced staff required. This division is now organized in three branches:

The Biology Branch sponsors research on the effects of atomic energy on animal and plant life and also research conducted with atomic energy materials (radioactive and stable isotopes) into animal and plant physiology, particularly as they relate to the fields of agriculture and the treatment of animal and plant diseases.

The Medical Branch develops programs for safeguarding the health of employees and populations in and about AEC facilities; sponsors research on the mechanism, diagnosis, and treatment of radiation injuries and the use of radioisotopes in medicine; and supervises the Commission's cancer program and the work of the Atomic Casualty Commission in Japan.

The Biophysics Branch develops policies and standards for the detection and control of radiation and protection of personnel, control of contamination, disposal of radioactive material, and the training of personnel in all this work; sponsors research programs in biophysics.

The primary and basic task of the Commission's Division of Biology and Medicine, as indicated in the recommendations of the Medical Board of Review, was to survey the work being done, and the people who were doing it, throughout the entire Nation. There were, and are, desperately few competent scientific and technical workers and teachers in the field of the effects of radiation on living things. There are many thousands of questions that need urgently to be answered, thousands of kinds of research that need doing. The first necessity was to find out what work was being done, and where, and by whom, and—just as importantly--what work was not being done, and where it might be done, and by whom. Overriding all else, was the necessity of drawing competent new workers into the field and providing vigorous centers of research and study where they might be trained. The board had warned that, "a failure to assure the recruitment of an adequate number of able young men may easily prove an irreparable mistake." An "adequate number," at the most conservative estimate, means many thousands—many times the number working in the field today.

From the beginning, the Commission aimed to build its program of research and training in the two ways suggested by the Medical Board: through continuing programs inside its own installations and laboratories and also through contracts with outside institutions for specific projects. From the Commission's point of view, each method has its special advantages, and neither would meet the needs of the situation alone.

THE PROGRAM IN RESEARCH

As the result of the wartime necessity of protecting atomic energy workers, strong organizations for research had been built up at a number of points:

METALLURGICAL LABORATORY, University of Chicago (now the Argonne National Laboratory).

CROCKER AND DONNER LABORATORIES, University of California.

CLINTON LABORATORIES (now the Oak Ridge National Laboratory), Oak Ridge, Tennessee.

HANFORD ENGINEER WORKS, Richland, Washington.

UNIVERSITY OF ROCHESTER, Atomic Energy Project, Rochester, N. Y.

Each one of these is now a center of activity in the developing program, as also is Brookhaven National Laboratory on Long Island.

The three AEC National Laboratories—Argonne at Chicago, Brookhaven on Long Island, and Oak Ridge in Tennessee—all have strong departments of biology and medicine and fully rounded, long-term programs of research and training. The laboratories at Los Alamos, Hanford, University of California, and University of Rochester also have long-term programs of more specialized nature.

These Commission laboratories are essential in carrying out a strong Nation-wide program in the biological and medical aspects of atomic energy.

(*a*) They serve as centers of research, training, and information. Close to 60 universities and other institutions participate in the work of the three national laboratories. All AEC laboratories have arrangements whereby scientists and students may visit and join in the work.

(*b*) They provide equipment not otherwise available. Private institutions cannot build nuclear reactors, and few of them can afford the large particle accelerators, the radiation chemical laboratories, and the other tremendously expensive equipment of atomic science. The AEC research centers are being extensively equipped to make such facilities available to scientists in all parts of the Nation.

(*c*) They provide secure locations for classified research. Although most of the biological and medical research in atomic energy is unclassified, there are programs which must be kept secret; and special restricted areas in AEC laboratories are set aside for such work, accessible only to cleared personnel.

Contract Research

Government laboratories have their essential place in the atomic energy program, but they alone could not carry forward the large-scale Nation-wide scientific advance needed today. American science has grown in private institutions. It is the universities that have the majority of the scientists, the tradition of achievement in free, imaginative research, and the teachers who are able to inspire and prepare the scientists of tomorrow. The Commission's program of research assistance has been planned to strengthen the biological and medical work of private institutions.

During the war, relatively few universities took part in the program. Notable among these were the University of Rochester, the University of California, Washington University (St. Louis), University of Washington (Seattle), University of Chicago, and Columbia University. Today, there are more than 100 projects in unclassified biological and medical research being carried out in more than 60 universities, hospitals, and institutions in all parts of the United States, under sponsorship of the Commission. (See pp. 537-48 for brief descriptions of the work.) Many of these are projects that were originally chosen for research support by the Office of Naval Research and are still administered through that organization. Others have been contracted for directly by the Commission.

Before letting contracts, the Commission carefully reviews proposals for research projects from five points of view, asking: (*a*) whether the proposed investigation falls within the general area where Commission support is justified; (*b*) whether it is scientifically sound; (*c*) whether the scientists who proposed doing the work are the best qualified that could be obtained for the particular project; (*d*) whether the institution is the best fitted for the work; and (*e*) whether the carrying out of the project at this particular place by those particular workers will be likely to result in adding to the number of scientists and students who become interested in the atomic energy aspects of biology and medicine.

AEC does not always wait for new projects to be proposed. In taking an over-all view of the work being done throughout the Nation—as it must do if it is to carry on its responsibility—it often sees the need for some key investigation. When this happens, AEC seeks out

qualified workers and seeks to persuade them to submit a proposal to do the work.

Other Federal agencies, of course, support research in atomic fields. The Armed Services, for example, investigate such problems as detection of radiation hazards, protection, and decontamination, as well as studies in what constitutes a fatal dosage of radiation under varying conditions, the injuries that come from radiation exposure, and how to treat them.

TRAINING AND INFORMATION PROGRAMS

Training is an inseparable part of scientific research A very large number of advanced students in biology and medicine receive training in connection with the more than 100 research contracts of AEC. Also, the national laboratories and other research establishments of the Commission, with their scores of associated universities, are being developed as centers of training as well as research. The Oak Ridge Institute of Nuclear Studies, associated with the Oak Ridge National Laboratory, and operated by 24 universities of the South under contract with the Commission, offers a variety of training opportunities, including a series of extremely popular courses in radioisotope utilization.

But the need for new scientists and technicians is so great that AEC has undertaken extensive programs devoted to training as a primary objective.

The fellowship program provides for 350 annual awards in the field of biology and medicine; 100 postdoctorals in medicine; 50 postdoctorals in biology; 175 predoctorals in biology and health physics; and 25 technical fellowships in health physics. Up to the present time, over 200 awards have been made.

During the past year, the Commission has expanded its previously existing activities at the various universities and colleges which are developing training programs in this field. These institutions were originally selected for their scientific competence and the opportunity to combine medical, biological, physical and mathematical programs, and their geographical location. During the past year all have offered courses for physicians including 10 representatives from the Armed Forces who were trained in the sciences which are basic to an understanding of atomic energy.

In addition, the educational opportunities in these centers serve as stimulants to their student bodies to become interested in the field

as demonstrated by the number of applications for fellowship training which were received from these institutions. It is anticipated that the number of students and the variety of program for teaching will be continually expanded in these institutions. Because of their geographic distribution and the competence of their faculties, they would in time of national emergency serve as valuable centers for training civilian and military personnel on a large scale.

Dissemination of Information

The Commission has a growing program for circulating technical information to scientists and technicians both inside and outside the national atomic energy project. In addition to making maximum distribution of papers resulting from current research, technical information personnel are engaged in the tremendous labor of sorting, indexing, and evaluating the backlog of scientific papers accumulated during the war and declassifying all that can now be released for the use of the scientific community as a whole.

The thousands of papers that must remain classified are distributed within the project to qualified personnel. Most of the publishable scientific results will be included in the National Nuclear Energy Series, the declassified portion of which will run to about 60 volumes of 500 or more pages each. The first of these volumes, "Histopathology of Irradiation from External and Internal Sources," was published in December 1948. Publisher for the unclassified volumes of the series is the McGraw-Hill Book Co.

Scientists and technicians in the atomic energy program require more than classified material, they also must have quick access to a wide range of unclassified papers originating both inside and outside the project. To provide this service, the Commission prepares a semimonthly publication, "Nuclear Science Abstracts." It is in wide demand by Government agencies, cooperating universities, and research laboratories, depository libraries of the Library of Congress, and other institutions of service to scientists. The demand from hospitals, medical schools, and medical research institutes reached such a point during the year that a special distribution to 1,200 such institutions was undertaken as a permanent part of the circulation. In addition to containing abstracts of existing articles, the Nuclear Science Abstracts also contain reviews on applicable scientific topics which are written by research scientists who are working in the radiation field.

Several of the Atomic Energy Commission laboratories have held symposiums for scientists at the affiliated universities. These meetings have ranged in length from 1 day to 3 weeks.

ACTIVITIES IN CIVIL DEFENSE

The Atomic Energy Act of 1946 assigns a number of functions to the Commission, which are pertinent to civil defense.

The Act requires the Commission (*a*) to establish controls over scientific and technical information relating to atomic energy in such a manner as to assure the common defense and security, (*b*) to make arrangements for research and development activities for utilization of fissionable and radioactive materials for medical, biological, health, or military purposes and for the protection of health during these activities, and (*c*) to establish standards and assist in training work required to protect health and to minimize danger from explosions.

Under these and other provisions of the Act, the Commission has specific responsibilities for the development of technical data needed by other agencies within the Government and for its public dissemination in accordance with policies established by the agency designated as responsible for civil defense.

The Commission has information on a number of pertinent problems and much of its research and development will apply to civil defense. It also contracts for related research in a number of colleges, universities and hospitals. The Commission can provide to the agencies information applicable to civil defense on ionizing radiation injury, shielding and shelters, medical care, training, and radiological safety—including instrumentation for the detection and measurement of atomic energy.

The Commission and the National Military Establishment are jointly sponsoring preparation of a special report on the effects of atomic weapons for public information, training of armed forces personnel, and basic civil defense. That report will contain data on blast, heat, and radiation effects, and will provide the basic material required for design of buildings to withstand such effects. It will also have information on the medical effects of radiation, some of which have been discussed in earlier sections of this chapter. Other chapters will cover instrumentation, monitoring, and civil defense measures.

The Commission's training programs in biology and medicine are helping to develop the scientists, technicians, and teachers who will play key roles in the protection of the population against possible dangers from the release of nuclear energy in the future.

Biology and Medicine Research Contracts

Amherst College: H. H. Plough, Research in Radiobiology and Chemical Genetics.—Mutant strains of *Salmonella* will be produced by radiation and a study made of the biochemical mechanisms whereby the genes control metabolic or growth changes in bacterial cells.*

Battelle Memorial Institute: K. S. Chester, Use of Radioactive Indicators in the Study of the Mode of Action of Fungicides.—This investigation is designed to elucidate the mode of action of fungicides by the use of radioactive tracers in fungicides and related compounds to fungus spores. It is planned to study the basic factors of just how fungicides, in the immediate environment of the spore, get into a position to exert their toxicity and specifically how such toxicity acts on cellular components of the spore.

Baylor University: Joseph H. Gast, The Use of Radioactive Sulfur in Studies on the Chemistry and Metabolism of some Sulfur Oxides.—Sodium thiosulfate, tetrathionate and dithionate and other intermediates will be prepared in labeled form and administered to dogs, rats, and rabbits. The percentage oxidation will be determined on the urine, and residual radioactive sulfur in tissues determined chemically and histologically.

Boston University: R. C. Crafts, The Hypophysis and Iron Metabolism.—Function of the hypophysis in the utilization of iron in hematopoiesis with radioactive iron in rat. Includes effects of gastric and intestinal acidity.*

California Institute of Technology: G. W. Beadle, The Genetic and Cytological Effects of High Energy Radiation.—This work is divided into work with *Neurospora Crassa*, *Drosophila* melanogaster and *zea mays*, or corn. Mutant strains of *Neurospora* and *Drosophila* produced by radiation are being studied to determine the exact chemical process that is interfered with by the genetic change. In corn the chromosome rearrangements produced by exposure to the Bikini tests are being studied for a critical comparison with X-ray treatment. The work with corn includes a genetical biochemical study of the development of the endosperm.*

California Institute of Technology: H. Borsook, Biological Synthesis of Proteins with the Use of Isotopes.—The mechanism of the biological synthesis of proteins using C 14 labeled intermediates is being investigated. Homogenates of liver and other tissues are used for synthesizing peptides. The effect of feeding diets low in certain amino acids on the *in vivo* synthesis of peptides and proteins will be studied.*

Cedars of Lebanon Hospital: Paul E. Rekers, Relationship of Flavanoid Structures to Radiation Protection.—To study further the protective action of selected chemical compounds on the course of irradiation disease, and to explore the mode of action, or mechanism of action of these compounds.

Columbia University (Barnard): Aubrey Gorbman, The Biological Effects of Radiation from Excessive Amounts of Radioiodine.—This project investigates

*Contracts administered through the Office of Naval Research, Washington, D. C.

whether thyroid hormone synthesis develops in a stepwise manner or if the ability to form new hormone develops suddenly. The studies include: (1) The effects upon the thyroid and neighboring tissues of radiotoxic doses of radioiodine; (2) An analysis of the function of the thyroid on unborn mice.*

Columbia University: David Nachmansohn, Effects of Exposure to Radioactive Material and X-ray irradiation on Nerve Tissue.—A study using radioactive isotopes of the effect of beta particles and gamma rays on nerve structure and function using the single nerve fiber of the giant squid. Especially concerned with effect of radiation on reaction of nerve to pharmacological agents.*

Columbia University: Sidney C. Werner, Use of Radioactive Iodine in Developing Quantitative Assay Method for Thyrotropic Hormone.—To develop by means of *in vitro* technique, using radioactive iodine, an adequate assay method for detection of the thyroid-stimulating hormone of the pituitary (TSH) in the blood and urine, in order to determine if this hormone is a causative factor in toxic goiter and malignant exophthalmos. Also to determine rates of secretion of thyroid hormone by direct determination of the radioactivity of total and protein-formed fractions of blood iodine, after injection of TSH into patients having anorexia nervosa, destructive lesions of the pituitary and adrenal glands, and patients after toxic goiter therapy, and into normal subject. The induced rate of secretion of the hormone may offer a better index of thyroid function than simple radioiodine uptake or basal metabolism measurement.

Connecticut Agricultural Experiment Station: A. E. Dimond, Therapy of Plant Disease by Nuclear Radiations.—This study will utilize radioactive materials as tracers to permit more detailed understanding of the action and movement of possible chemotherapeutic materials and will also explore the possibilities of the use of radiation from radioactive materials as direct therapeutic agents in diseases of plants.

Duke University: Philip Handler, Metabolic Studies with Radioactive Isotopes.—Use of radioactive phosphorus in studying turn-over rates for organic phosphates of renal tissue as affected by hormonal factors. Use of ion exchange resins in fractionations of organic phosphates. Use of radioactive sodium and potassium in studies on dehydration, acidosis, and alkalosis.

Duke University: K. M. Wilbur, I. The Isolation and Membrane Permeability of the Liver Cell Nucleus.—(A) Better techniques for the isolation of rat liver nuclei free from other cell components; (B) Study of the permeability of the isolated nucleus utilizing radioactive tracers; (C) Method of evaluating extraction techniques. II. Shell Formation in Molluscs and Barnacles as Studied by Radioisotopes.—Use of radioactive calcium and phosphorus to study the growth of shell formation using oysters and barnacles and the determination of the rate of growth within periods of hours and days.

Harvard University: O. Cope and F. Moore, The Use of Radioactive Isotopes in Studies on Fluid, Protein, and Electrolyte Requirements.—Study of total body water and solids by isotope dilution technique including measurement of total exchangeable potassium by radiopotassium and measurement of total body water with heavy water. Histochemical methods to verify findings with radioisotopes.*

Harvard University: H. L. Blumgart, Radioactive Therapy of Graves' Disease.—Use of radioactive iodine in therapy in Graves' disease and other thyroid disorders.*

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Harvard University: A. B. Hastings et al., Research with Isotopes on Medical Problems, Training in Isotope Techniques, Research on Enzyme Action, Metabolism of Organic Compounds in Mammalian Systems. Use of Radioisotopes as Diagnostic and Therapeutic Agents in Malignancies.

Harvard University: Karl Sax, Dosage Curves Under Varying Conditions of Time and Intensity of Radiation.—The cytological effects of X-ray and the short wave radiations are being investigated, as are the effects of various secondary factors such as low temperature, infrared, and supersonic radiation on chromosomal aberrations.*

Harvard University: J. H. Shaw, R. F. Sognnaes, Studies on the Metabolism of the Teeth with Special Regard to Radioisotope Studies on the Enamel.—To elucidate the question of normal and abnormal changes in the enamel, dentine, and cementum during formation and function, using radioisotope tracing method.

Henry Ford Hospital: F. W. Hartman, The Chemical Sterilization of Blood and Plasma with Nitrogen Mustards.—To eliminate the possibility of homologous serum jaundice from the administration of blood or plasma. Records kept of all clinical cases receiving plasma and blood treated with HN_2. Each clinical case receiving HN_2 treated plasma observed for immediate or delayed allergic manifestations.

Howard University: Herman Branson, Metabolism of Radioactive Isotopes.—Studies are being made of the metabolism of radiophosphorus 32, radioiodine 131 and radiocobalt 60 in rats.*

Johns Hopkins University: Abel Wolman, Investigation of Adsorption and Assimilation of Radioactive Waste by Bacterial Slimes.—Bacterial slimes are usually found in all types of plumbing systems. This study is investigating the extent to which such slimes concentrate radioactive wastes passing through the plumbing system.

Long Island Biological Association of Cold Spring Harbor: M. Demerec, Study of the Accumulation and Elimination of Deleterious Gene Mutations in Experimental Populations Exposed to Radiations.—This project concerns the accumulation of lethals, semilethals, viability modifiers, and their elimination by natural selection in populations (*Drosophila*) exposed chronically to relatively small amounts of radiation or to single high levels of radiation.

Massachusetts General Hospital: J. H. Means, The Effects of Radioactive Iodine on the Biology of the Thyroid Gland.—Study of radiation effects both early and late by biopsy of thyroid of patients of the Thyroid Clinic of the Massachusetts General Hospital. The effect of repeated tracer doses upon the biology of the normal human gland also to be studied.

Massachusetts Institute of Technology: R. D. Evans, Chemical Content of Blood Cells as Determined with Radioisotopes.—A study on the role of iron and zinc in normal development of red and white blood cells with the application of this knowledge to the development, diagnosis, and treatment of blood dyscrasias.*

Massachusetts Institute of Technology: R. D. Evans, Radiomedicine Research.—Radioactive isotopes are produced, chemically separated and standardized, and prepared in a form suitable for medical research. Instruments are being studied and developed to provide a more efficient utilization and measurement of the isotopes.*

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Massachusetts Institute of Technology: A. A. Thomas, Efficiency of Present Water Treatment Methods in Removing Radioactive Substances from Water.—Research is underway to explore the effectiveness of water treatment processes now in use for the removal of radioactive materials from drinking water.

Massachusetts Institute of Technology: J. C. Trump, Sterilization of Foods and Drugs with High Energy Cathode Rays.—In this study, the effects of high energy X-rays in bacterial enzymes, vitamins, spores, and other organic forms will be investigated. Attempts will be made to improve methods for using such radiations to sterilize foods and drugs, to determine whether these high energy radiations will harm these foods and to determine the economic practicality of large-scale use of these methods.*

Meharry Medical College: Paul Hahn, Treatment of Neoplasms.—Therapeutic and diagnostic studies of malignancies with use of isotopes, particularly colloidal gold 198.

Memorial Hospital: C. P. Rhoads, Cancer Research.—Part I.—Investigations Involving Use of Isotopes and Radiation in the Study of Protein Chemistry, Physics, Experimental Pathology, Immunochemistry, Immunology, and Special Tumors. Part II. Distribution of Isotopes in Therapy.*

Michigan State College: L. F. Wolterink and E. P. Reineke, Hormonal and Nutritional Factors which Alter the Effective Half-Lives and Different Absorption Ratios of Calcium and Phosphorus.—Thyroid and sex hormones in various combinations and their effect on the absorption and excretion of calcium, manganese, and cobalt are being studied as well as the rates of turnover of these elements in the liver, bone, and other tissues as affected by hormones.

Mount Sinai Hospital: M. Loevinger, Measurement of Tissue Dose Due to Gamma and Beta Active Radioisotopes.—Present dosage standards for use of radiation in therapy have been based on X-ray and radium. The present study is one of a series financed by the AEC to determine comparable dosage standards for radioactive cobalt (cobalt 60) which has been suggested as an inexpensive substitute for radium in the treatment of cancer and other diseases requiring radiation.

National Research Council: Radiation Cataract Investigation.—Investigation of the ocular changes related to cyclotron exposures.

New York University: Marion Sulzberger, Skin Changes Produced by Low Voltage Roentgen Ray Irradiation.—To determine possible influence of low voltage X-irradiation for treatment of dermatoses, upon incidence of skin cancers in some patients 2–12 years after therapy.*

North Carolina State College: W. C. Gregory, The Effects of the Irradiation of Peanut Seed.—The possibilities of inducing mutants of value is being investigated by irradiation of seeds with appropriate levels of ionizing radiation. Progeny of irradiated seeds will be studied for chromosomal, morphological, and resistant mutants.

North Carolina State College: N. S. Hall, The Movement of Ions through Soil Systems.—This is a study of reactions of ions at solid-liquid interface, soil anion and cation reactions, and the rate of isotopic movement in soils.

North Carolina State College: H. T. Schofield, Permeability of Certain Epidermal Membranes to Gaseous Carbon Dioxide.—Using C 14 O_2, studies are being made on the permeability of cutinized epidermal walls of the leaves and

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fruits of several species of plants and the permeability of epidermal cells of roots.*

North Carolina State College: J. A. Weybrew, Metabolism of Copper.—The absorption, distribution, metabolism, and excretion of copper during pregnancy and lactation is being studied using radioisotopes as tracers in rabbits and other animals.*

Northwestern University: J. Roscoe Miller, Radioisotope Unit for Investigation, Research, and Therapy.—Establishment of a radioisotope unit at Northwestern for: (A) Training of undergraduate and graduate students in use of isotopes in research, therapy, instrumentation, and radiological safety. (B) Provide isotopes for clinical therapy and research.*

Ohio Agricultural Experiment Station: R. S. Davidson, Physiology and Genetics of Plant Pathogenic Micro-organisms When Grown in the Presence of Various Radioisotopes.—Studies are being made on the physiological and genetic response of selected plant pathogenic organisms to radiations from radioisotopes. The possibility of using radioisotopes for tagging spores of certain plant pathogenic organisms to facilitate ecological and epidermiological solutions to disease problems is being investigated.

Ohio State University: J. L. Morton, Use of Radioactive Cobalt 60 and Other Radioisotopes for Treatment of Cancer.—This study was proposed to develop the physical principles underlying the use of radioisotopes as a substitute for radium or X-ray in the treatment of cancer and allied diseases. Methods for measuring the radiation dosage will include use of photographic films and small ionization chambers having outside diameters as small as 5 millimeters.*

Ohio State University: M. L. Pool, Studies of Radioautographic Techniques.—Propose to study methods and techniques of sharpening radioautographs by use of a very strong magnetic field.*

Oklahoma Agricultural & Mechanical College: A. Eisenstark, Study of Cytogenetic Effect of Irradiation, Using Radioactive Isotopes on Bacteria.—Radiophosphorus will be used to release energies within bacterial cells. *Azotobacter chroococcum* exposed to various levels of radiation will be examined for cytological changes by means of the electron microscope, phase microscopy, and other techniques.

Oregon State College: J. S. Butts, The Mode of Action of 2-4 Dichlorophenoxyacetic Acid as Studies with the Use of Carbon 14.—This project is designed to provide information on the mechanism whereby 2-4-D exerts its selective herbicidal effect on some noxious plants.*

Oregon State College: V. H. Cheldelin and B. E. Christensen, A Study of Vitamin-Amino Acid and Carbohydrate-Amino Acid Interrelationships Using Carbon 14 as a Tracer Substance.—By employing biosynthesis for the incorporation of tagged molecules into the tissues of rats and cells of micro-organisms the mechanism of synthesis and metabolism of amino acids and vitamins will be investigated. The distribution of C 14 in amino acids, vitamins, and various intermediary metabolites is being determined.*

Purdue University: H. Koffler and P. A. Tetrault, The Use of Radioactive Isotopes in Studying Mold Metabolism with Emphasis on the Assimilatory Mechanisms of *Penicillium Chrysogenum.*—The metabolism of various organic nutrients such as acetate, citric acid, and fatty acids by molds and the effects of rates of

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oxidation on endogenous respiration are being investigated using radioisotope tracers.*

Reed College: J. P. Hungate and A. H. Livermore, I. Application of Radioactive Techniques in the Field of Cellular Metabolism.—The *in vivo* synthesis of serine and glycine and their interconvertibility are being studied, employing as the metabolic agent a strain of *Neurospora* in which the synthesis of serine and glycine can be modified genetically. II. Biological Synthesis of the Peptide Bond.—Radioisotopes will be used to label various organic compounds and particularly the amino acids in the mechanism of synthesis of the peptide bond.

Rice Institute: A. C. Chandler and R. V. Talmage, I. The Nutrition of Tapeworms. II. Relaxin in Blood.—The nutritional requirements of the tapeworm using rats as the host animal is being studied. The uptake by the tapeworms of various nutrients labeled with radioisotopes when administered to a normal host and to a host deficient in the nutrient. The function of relaxin, a hormone from the *corpus luteum*, is being studied with animals receiving Fe 59, P 32, and C 45.

Simpson Memorial Institute: Frank H. Bethell and Cyril S. Sturgis, Preliminary Study of the Survival of Red Blood Cells after Treatment with Nitrogen Mustard.—Preliminary study using the Ashby Technique and possibly undertaking the method involving radioactive isotopes. The purpose of the work is to develop a chemical method for sterilizing blood to be used for transfusions and to decrease the incidence of transfusion reactions.

Southern Research Institute: H. E. Skipper, Body Retention of C 14.—Various radiocarbon compounds are administered to experimental animals and the retention of the active carbon in bone and soft tissues determined. The effect of the retained C 14 on the occurrence of neoplastic conditions and on the formation of hemoglobin are being determined.*

Trudeau Foundation: F. W. Klemperer, Experimental and Clinical Studies Involving Beryllium and Berylliosis.*

Tufts College: David Rapport, The Effects of Radiation Associated with Growth.—Effect of radiation and monochromatic ultraviolet light on normal and abnormal tissue homogenates, as indicated by alterations in the synthesis of ribose, and desoxyribose-nucleic acid—especially from histidine and pyrimidines.*

Union College: L. B. Clark, Biological Effects of High Voltage Radiation.—The biological effects of one million to 100 million volts produced by the synchrotron and betatron. The effect on physiological functions of the cells and enzyme systems of various levels of radiation are being studied. New techniques will be developed with micro-organisms and then extended to laboratory animals.*

U. S. Department of Agriculture: R. M. Salter, The Improvement of Soil Management and Crop Production Through Investigations with Isotopes.—The objectives of this research project are to develop procedures for the safe and effective use of radioisotopes in soil and crop research, to characterize the plant nutrient and nonessential reserves in soils and to determine the mechanism and rate of release of these reserves to crops under various conditions through use of radioactive materials and to study by means of radioistopes the uptake and accumulation of essential and nonessential elements by various crop plants.

University of California: Hermann Becks, Studies on the Metabolism of Radioactive Fluorine with Particular Reference to Dental and Skeletal Structures.—(1)

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To study adsorption of F 18 by teeth with and without caries *in vivo* and *in vitro*, and by teeth with and without periodontitis; (2) Metabolism of fluorine; and (3) Kinetics of F 18 uptake by the skeleton from blood under various experimental conditions.

University of California: Max Kleiber, Metabolism and Biological Synthesis with Large Animals.—The metabolic pathway of simple compounds such as lactate and pyruvate labeled with carbon 14 will be studied with lactating animals. The extent to which these labeled compounds appear in the protein, fat, and lactose of the milk are being determined. The biologically labeled constituents of the milk are being studied chemically and the components used for metabolism studies with laboratory animals.

University of California: A. P. Krueger, Air-borne Infections.—The aerosols of air-borne pathogens, relationship of local respiratory immunity and systemic immunity to inhaled and subcutaneously injected antigens, the effect of whole and partial body radiation on susceptibility to infection are being investigated.

University of California: J. H. Lawrence, Immediate and Delayed Biochemical and Biological Effects of Irradiation on Animal Tissue.—To develop methods of causing radioactive materials to be selectively deposited in tissues, especially the lymphatic tissues. Specifically irradiated spleen, liver, and bone marrow will be investigated individually, with particular reference to biochemical assessment of tissue metabolism changes and possible relation to histological changes. Survey will be made of some of the enzyme systems within the body which may be impaired by *in vivo* irradiation. Also study of the responses in plasma protein levels as they are affected by specific irradiation of liver, spleen, bone marrow, or lymphatic tissue and compared to whole body irradiation, including survey of the plasma protein functions by standard electrophoretic and ultra-centrifugation equipment.

University of California: Nello Pace, Use of Radiocarbon in Studies on Carbon Monoxide Physiology and the Implications Concerning Respiro-Circulatory Physiology.—A study of factors influencing elimination of carbon monoxide, the nature of the sex difference in rate of release of carbon monoxide, the feasibility of treatment of carbon monoxide poisoning in humans by oxygen under high pressure, rate of equilibration of labeled sodium and water in the body.*

University of Chicago: Paul C. Hodges, Studies in Radioautographic Techniques.—Studies will be made of methods of producing a sharper image in fluoroscopic work, and an effort is being made to devise a method for X-raying the small intestine with 35 mm. films.*

University of Chicago: C. Phillip Miller, The Bacteriological Aspects of Radiation Sickness.—Investigation of the effects of radiation on: (1) The animal host—using dogs and mice. The study is to include: *a* Effect of small doses of radiation, e. g. LD–50 and LD–25; *b* Systematic determination of bacterial flora at all levels of the gut; *c* Effect of various antibiotics on intestinal flora of normal and irradiated subjects and on bacteremia in irradiated subjects; and *d* Susceptibility of irradiated animals to infection. (2) Bacteria normally or potentially pathogenic for the host. *a* Induction by irradiation of easily detectable mutants; *b* Determination whether virulence can be enhanced by irradiation; *c* Production of bacterial endotoxin containing a tracer element.

University of Chicago: R. E. Zirkle, The Design and Construction of a Microbeam Light Atomic Nuclei for Biological Investigation.—The radio microbeam for

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biological investigations would have a cross section small in comparison with the single cell. Such a microbeam would permit selective irradiation of a part of individual cells and thereby contribute to the knowledge of cellular processes.*

University of Cincinnati: Robert Kehoe, Studies on Chronic Beryllliosis, Tumor Production by Beryllium, and Analytical Methods.—To determine quantitative relationship between dust inhaled and the lung changes. Analytical methods include increased sensitivity of the spectrographic method, development of adequate chemical methods, and analysis of beryllium ore dusts. The studies on tumor production will center about a repetition of Gardner's work.*

University of Colorado: Irving Goodman, Metabolism of Nucleic Acid Derivatives.—(1) Synthesis and biochemical study of tagged nucleic acid derivatives; (2) Crystallographic and optical properties; (3) Mechanism of radiation damage; and (4) Infrared absorption spectra.

University of Colorado: J. R. Lacher and Irving Goodman, Relationship of Structure and Biological Activity in the Intermediate Metabolism of Nucleic Acid Derivatives.—Micro-organisms growing in known media will be irradiated in the presence of certain metabolite antagonists. Pyrimidines will be synthesized with various substituted isotopically marked groups or elements. These will be added to a known medium and the protoplasmic constituents of the organisms assayed to determine their metabolic fate.

University of Colorado: T. Puck, Studies of the Radiation Chemistry of Bacteriophage Invasion and Reproduction of Host Cells.—This study is designed to gain an understanding of normal and radiation-induced mechanisms involved in the reproduction and mutation of bacterial viruses and their host cells. The viruses will be isolated and irradiated with ultraviolet and ionizing radiation and then allowed to attack susceptible cells.

University of Delaware: Mary A. Russell, Comparison of the Effects of X-rays, Neutrons, and Mustard Compounds on the Growth and Development of the Corn Seedling.—Effects on growth of roots of exposure to X-rays, neutrons, and mustard compounds are compared. The cytological effects of such treatments to growth types are being studied.*

University of Denver: Fred D'Amour, The Physiologic and Pathologic Effects of Radioactive Cobalt.—The physiological effects of the cobalt ion will be compared with those of the radioactive isotope. The effects of radioactive cobalt on various physiological processes such as hematopoieses, endocrine function, and production of carcinoma are being studied.

University of Illinois: B. C. Johnson and H. E. Carter, The Metabolism of Vitamins and Their Interrelationships with Amino Acids.—Vitamins and amino acids containing carbon 14 will be synthesized. These will then be administered to rats, chickens, pigs, and possibly other species. Their metabolism and the mechanism of their action in the animal body will then be studied.

University of Illinois: L. Ridenour, Construction of a Radiocobalt Applicator.—An applicator for giving whole-body radiation to mice is being constructed. It will be used to study the lethal effect of radiation in mice, decoloration of hair, radiation-induced changes in the brain and liver, and enzyme reactions in irradiated tissue.*

University of Kansas: E. R. Hall, Radium Chloride and Hemapoietic Physiology of Native Rodents.—Proposed to inject in rodents radium chloride intraperitone-

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ally at varying lengths of time, in varying amounts, to study the comparative effects (as shown by histological sections, and possibly also by breeding experiments and other means) on the spleen, lymph nodes, thymus, bone marrow, and possibly on the brain and reproduction organs.

University of Kansas: F. E. Hoecker, Studies of the Biological Effects of Ionization. The biological effects of electrons, neutrons, and alpha particles on cells are being studied and compared.*

University of Michigan: Fred J. Hodges, Radioautography.—The presence and location of radioactive materials concentrated in plant and animal tissue is recorded on photographic film when tissue slices are laid next to the film. The process, known as radioautography, is becoming a useful tool in medical diagnosis and biological research. This project will attempt to develop means for focusing beta ray emanations in order to give better definition to radioautographs.*

University of Michigan: Reuben L. Kahn and Fred J. Hodges, Universal Serologic Reaction Following Irradiation.—Performance of universal serological tests on patients before and after irradiation, and on animals before and after irradiation. Investigation of different lipid antigens in the universal serological technique; serum fractions in the universal serological technique; technical variations of the universal serological technique.

University of Minnesota: S. W. Hunter, Investigation on the use of Zirconium as a Radio-opaque Media.—To produce compounds containing zirconium, to investigate these for their radiographic properties; to test the toxicity of these compounds with intraperitoneal, gastrointestinal, and intravenous injections in mice, rats, dogs, and rabbits. Proposed to use the compounds on normal animals and animals with experimentally produced lesions.

University of Minnesota: George E. Moore, The Study of Methods and Instruments to Improve the Localization of Radioactive Materials in the Body with Special Reference to the Diagnosis of Brain Tumors.—Radioactive diiodofluorescein (I 131) is used in an effort to diagnose and localize brain tumors before operation. Also, attempts to use radio-opaque dyes for the localization of brain tumors by roentgenography, hitherto unsuccessful, are continuing. Investigation of sensitivity of various counters and counter systems including scintillation counters, development construction of multiple counter apparatus.

University of Minnesota: E. C. Stakman, The Effects of Radioactive Substances on Plant Pathogens and Other Micro-organisms.—The effect of radioactive substances in culture media on the production of valuable mutations in selected groups of micro-organisms of economic value is being determined. The cultural characteristics and physiology of induced mutants and the genetic effects of mildly radioactive substances on soil-borne plant pathogens will be studied.

University of Missouri: J. Levitt, The Translocation of Mineral and Iron Mineral Substances in Plants.—The mechanism and the rate of radiophosphorus absorption by plants, the effect of various factors on its uptake, its path of movement, and its quantitative distribution in the plant are being investigated.*

University of North Carolina: H. D. Bruner, The Use of Radioisotopes in Measuring the Volume Flow of Blood in Various Organs.—Will use radiokrypton and radioiodine labeled compounds to measure volume blood flow in liver and kidney.*

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University of North Carolina: Donald P. Costello, Radiation Effects on Salamander Larvae.—Research to elucidate some of the effects of radiation from radioisotopes on living cells, using the tail tip of the larval salamander for the study of chromosome numbers and mitotic figures.

University of North Carolina: C. T. Kaylor and C. D. Van Cleave, Radioautographic Study of the Distribution and Retention of Beryllium in the Rat.—To determine by means of radioautographic method, histological localization of tracer amounts of radioisotope Be 7 in tissues of the rat; also to investigate retention of the material over an extended period and under various experimental conditions. Following intramuscular or intraperitoneal injections of radioberyllium in an isotonic solution, animals to be sacrificed after 1, 4, 16, and 64 days; representative organs and tissues are fixed, embedded, and cut, with special attention laid on bone, liver, kidney, and hemapoietic system.

University of North Carolina: Arthur Roe, Carbon 14 Research.—To seek to determine whether C 14, by virtue of its greater weight than C 12 or its radioactivity, has any effect on the speed or on the course of organic reactions. A variety of reactions involving a symmetrical bifunctional reagent and "functional groups" differing only in that one will contain C 14 and the other C 12, will be carried out. Suitable clinical means will be employed to determine the degree of reaction with the "functional groups."

University of Oregon: John B. Graham, Response of Cells to Deep Radiation.—Detection of radiation injury as manifested by cytological changes in vaginal and oral smears.*

University of Oregon: P. L. Risley, Localization of Radioactive Isotopes in Germ Cells and Reproductive Tissues During Quiescence and Activation.—Investigation of germinal tissues with respect to their chemical and metabolic requirements by use of radioisotopes. Propose to administer radioisotopes to animal organisms of diverse kinds to determine if those now available can be demonstrated to localize in reproductive cells during different periods of relative quiescence and activity.*

University of Oregon: E. West, The Degradation of Radioactive Cholesterol, Fatty Acids, and Ketone Bodies in the Animal Body.—To study by the use of acetic acid labeled with carbon 14, the relation of ketone body formation to the hypercholesteremia and fatty liver condition of the diabetic state.*

University of Pennsylvania: D. Wright Wilson, The Synthesis of Isotopic Carbon Compounds Used in Biochemistry.—Study of the intermediary metabolism of various substances by using radioactive carbon as a tracer.

University of Rochester: Herman E. Pearse, A Study of the Thermal Effects of the Atomic Bomb with Special Reference to "Flash Burns."—The program covers a complete study of the characteristics and effects of flash burns on the total organism leading to an understanding of the changes in physiology, pathology, and blood chemistry, and eventually to a means of mastering the problem of therapy in a clinical sense.

University of Rochester: G. H. Whipple, The Investigation of Plasma Proteins with Isotopic Labeled Amino Acids.—The role of the plasma proteins as intermediaries in the protein metabolism of the human body. This includes labeled lysine and labeled carbonate and the development of routine quantitative methods of high sensitivity for C 14 determinations on tissue and tissue fractions. Studies

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on preparation of epsilon-amino-alpha-hydroxy caproic acid and methionine labeled with carbon 14 as the gamma carbon.*

University of Tennessee: F. S. Chance, The Effects and Use of Radioisotopes and of Radiation on Animals.—Breeding and growth studies with cattle exposed to the dust "outfall" from the bomb at Alamogordo and histological and pathological studies of the tissues from some of these cattle. The use of radioisotopes in metabolism studies of farm animals will be investigated.

University of Texas: Jack Myers, Biological Accumulation of Inorganic Materials by Algae.—The isolation, identification, nutrient requirements, and the effect of various environmental factors on rates of growth are being studied on various strains of algae. Studies will also be made on the accumulation of radioactive inorganic materials.*

University of Virginia: A. Chanutin, The Effects of X-Radiation on the Plasma Proteins.—Determine effect of radiation on plasma protein distribution of rats by ethanol fractionation procedures of *Cohn*. The cholesterol, phospholipide and total lipid carbon of these fractions will be determined.*

University of Virginia: Chalmers L. Gemmill, The Effect of Beta Radiation on the Distribution of Phosphate in Red Blood Cells and in Cardiac Muscle.—A study of the transfer of radioactive phosphorus from the plasma into the red blood cell under the influence of various anesthetics, including a study of phosphate distribution between the various carbohydrate factors in the red blood cell and in the beating isolated heart.

University of Washington: Clement A. Finch, Isotope Studies in Iron Metabolism.—Comprehensive approach to certain problems in iron metabolism, using isotopes for study of iron absorption, turnover of various tissue iron fractions, erythropoiesis, red cell viability, and red cell breakdown.

University of Washington: R. H. Williams, An Investigation of the Biological Effects of Radioactive Sulfur.—(1) Determine specific structural types of organic sulfur compound which localize in adrenal gland; and (2) Determine general tissue distribution and histological changes resulting.

University of Washington: J. A. Miller, Labeled Azo Dye Research.—Synthesis of carcinogen 4—dimethyl amino azobenzene.*

Wake Forest College: Camillo Artom, The Use of Radiophosphorus in studying Hormonal and Pharmacological Actions on the Formation of Tissue Phospholipides.—Use of intact animals and isolated tissue slices in studying various factors affecting phospholipide metabolism. The intermediate compounds will be identified by the use of enzyme inhibitors, and the relationship between the metabolism of phospholipides and that of proteins and fats determined. The substances to be used include BAL, alloxan, phyloxyin, thiourea, insulin, thyroxine, etc.

Wake Forest College: G. T. Harrell, The Distribution and Turnover of Radioactive Sodium and Potassium in Acute Infections.—Comparison of sodium and potassium distribution and turnover as indicated by radioactive isotopes and by ordinary biochemical procedures. Applications to fluid balance studies in Rocky Mountain Spotted Fever and serum sickness.

Washington State College: Orlin Biddulph, The Absorption, Translocation and Deposition of Various Elements in Plants.—This project involves the absorption

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of tagged elements from an external nutrient solution, the distribution pattern of the element in the plant tissues, and the recirculation via the phloem tissues.

Washington State College: N. Higinbotham, The Rate of Movement of Ions Into and Through Plant Parenchyma Tissue as Affected by Rate of Water Uptake.—A study of the rates, extent of accumulation, and mechanism of movement of ions in homogeneous plant tissue. The possible relation of rates and direction of water movement to salt movement in homogeneous plant tissue are being studied.

Washington University: W. Allen, Use of Gamma-Ray as a Therapeutic Agent in Carcinoma.—Use of colloidal gold 198 as a gamma-ray emitter in carcinoma therapy.*

Washington University: David Lipkin, Study of Nucleic Acids, Nucleoprotein, Nucleotides and Related Organic Phosphorus Compounds.—Research involves the synthesis of ribonucleotides containing C 14; development of a method for this synthesis of desoxyribonucleotides; application of a synthetic method for the preparation of desoxyribonucleotides to the preparation of such molecules containing C 14; development of methods of isolating undegraded nucleic acids from various tissues and organisms; and study of the structure of undegraded nucleic acids isolated from various sources.

Washington University: Wendell Scott, Experiments to Determine the Feasibility of Developing Equipment that will be capable of Mapping the Outlines of Organs or Deposits of Metastatic Tumor Within the Body.—X-ray examination of many body organs such as the pancreas and spleen is difficult because the transparency of the organic tissue leaves no shadow on the X-ray screen or plate. If such organs could be made to concentrate tracer amounts of radioactive material, it would be possible to map the outline of the organ by use of electronic instruments. This project proposes to study the extent of the concentration of radioactive materials in body organs, and methods of instrumentation necessary for "mapping" the outline of the organ.*

Western Reserve University: H. G. Wood, The Intermediate Metabolism of Carbohydrates by Bacteria.—(1) To determine if ATP is a necessary component for fixation of carbon dioxide in oxalacetate with enzymes from bacteria; (2) The conversion of pyruvate to acetyl methyl carbinol lactic and acetic acids, and the fixation of carbon dioxide will be studied; (3) Determine if acetyl phosphate is an intermediate in the conversion to carboxyl of pyruvate; (4) Role of acetate condensation in the formation of succinate and its significance in respiration.*

Yale University: E. C. Pollard, Monomolecular Layers of Seriological Agents.—The physical and biological effects of irradiating films of proteins with protons, electrons, gamma and other rays.

Yale University: E. C. Pollard, The Irradiation of Viruses and Large Molecules.—The effect of deuterons of variable ionizing density on biological molecules such as pepsin and ascorbic acid. This study is designed to obtain information on the biological effects of deuterons.

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The Battle of the CONSCIENCE

by

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Dr. Edmund Bergler has been in private practice as a psychoanalytic-psychiatrist in Vienna and New York since 1927. A graduate of of the Medical School of the University of Vienna, he was on the staff of the Psychoanalytic Freud-Clinic in Vienna from 1927 to 1937, serving the last four years as assistant director. In 1942-43 and 1944-45 he was a lecturer at the Psychoanalytic Institute in New York.

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CITY AND STATE .....

The year that got away—

LONG AGO, he'd planned the year, the day, the hour of his retirement.

But now, a year beyond that date, his desk is still open . . . the weekday trout still in the brook.

What happened? Unexpected expenses . . . Nickie starting college . . . the last of Mom's hospital bills. He never really figured it out. But the happy day he planned was no longer in sight.

A lot of years are getting away from a lot of people . . . because they don't have a plan which helps them save money *regularly*. But there *are* people who are making the most of the years, by investment in United States Savings Bonds.

It's an easy, automatic way of insuring a financial future, thanks to two simple, *automatic* plans:

1. The Payroll Savings Plan, at the firm where you are employed. You get a bond just as often as you like.

2. If not on a payroll, join the Bond-A-Month Plan at your bank.

Don't let another year—another moment—escape *you*. Sign up today.

Automatic saving is sure saving—
U.S. Savings Bonds

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30-DAY TEST REVEALED

"Not one single case of throat irritation due to smoking Camels!"

Yes, that's what throat specialists reported after making weekly examinations of the throats of hundreds of men and women from coast to coast who smoked Camels, and only Camels, for 30 consecutive days.

R. J. Reynolds Tobacco Co., Winston-Salem, N. C.

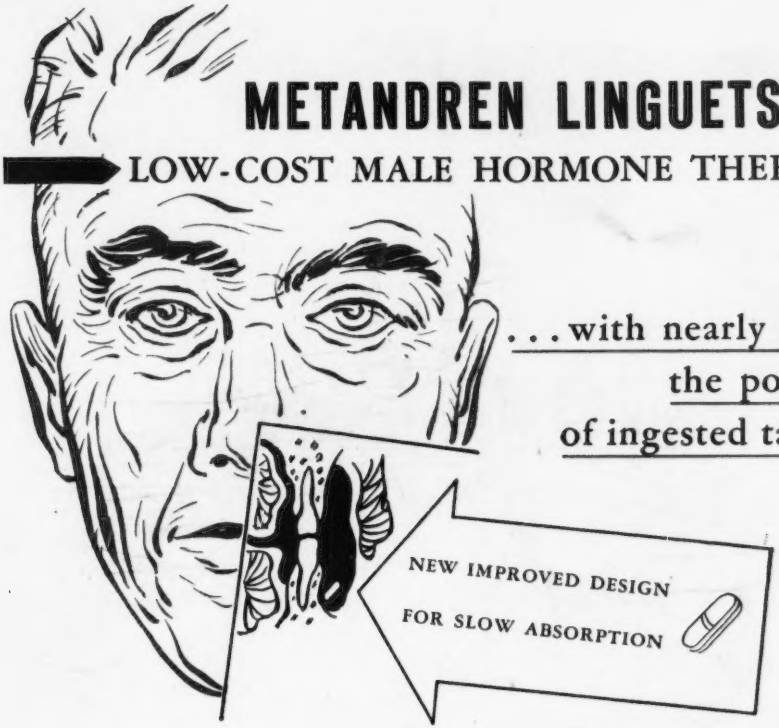
According to a Nationwide survey:

More Doctors smoke Camels than any other cigarette

When three leading independent research organizations asked 113,597 doctors what cigarette they smoked, the brand named most was Camel!

METANDREN LINGUETS

LOW-COST MALE HORMONE THERAPY



. . . with nearly twice the potency of ingested tablets

Metandren Linguets contain methyltestosterone for sublingual or buccal administration.

The superiority of Metandren Linguets over other androgens by this route may be partly attributed to the fact that only methyltestosterone is effective orally. In contrast, when free testosterone or testosterone propionate is given sublingually, that portion unavoidably swallowed is almost completely destroyed.

Metandren Linguets of methyltestosterone are the "most economical and also efficient way of administering testosterone," according to Lisser.[1] Tyler finds that 140 mg. of methyltestosterone weekly in the form of Linguets is equivalent to an ingested dosage of approximately 210 mg., or to an injected dosage of 75 mg. of testosterone propionate.[2]

PERANDREN
is the pioneer brand of testosterone propionate, the most potent injectable androgen.

Adult maintenance dosage is from one to three 5-mg. Linguets daily. Most children need only one-half to one 5-mg. Linguet daily. Literature on request.

1. Lisser, H.: Calif. & West. Med., 64: 177, 1946
2. Tyler, E. T.: J.A.M.A., 139: 9, Feb., 1949.

METANDREN LINGUETS, 5 mg. (white), scored; 10 mg. (yellow), scored – in bottles of 30, 100 and 500.

Ciba PHARMACEUTICAL PRODUCTS, INC., SUMMIT, NEW JERSEY

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